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Rocky Mountain Medical Journal

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January 1975

VOLUME 72 • NUMBER 1

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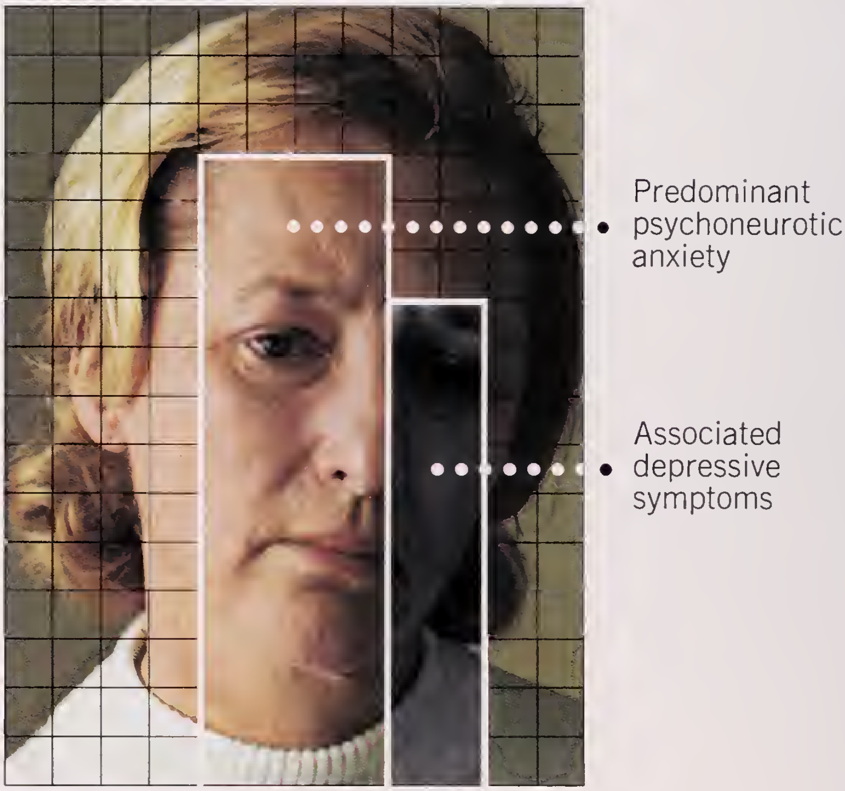
Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/ or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/ or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

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in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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OUR COVER

The envy of skiers the world over, Colorado snow is both platform and outer space; a speed-maker when ski meets trail or new snow, a spinner of gossamer exhilarations when the snow and sun and sky come together as in this evocation of all that makes Colorado skiing so extra special. Photo by Russell/Dabney. Credit: Colorado Ski Country USA.

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Letters TO THE EDITOR

To the Editor:

For many years I have read with interest the reports of the Colorado Maternal Mortality Committee. I note with interest that although anesthesia is frequently involved in the reports—No Anesthesiologist serves on the committee and frequently the anesthesia management of the particular case under study is missed or ignored.

The case reported in the October 1974 journal might be a case in point. Whereas, I agree that the primary cause of death is due to the patient's religious convictions regarding Blood and Blood products, I do question some of the management aspects of the case. I would like to have had more details as to the caudal anesthesia-drug used and level and the agents used for the D and C and subsequent Hysterectomy. I also question the fluid management as detailed in the summary. From the reports I wonder if there was sufficient I.V. fluid replacement. If not, the Mannitol and Lasix was only "whipping a tired horse" in view of inadequate circulating volume.

From the report there is good reason to believe that the patient probably could not have been saved. But there is always that hope and also the concern that the medical management did not contribute to this patient's demise.

If our Journal is to report cases such as this—How much better would it be to examine all facets of the problem. Certainly the committee as constituted is capable, but wouldn't it even be a more effective committee and more informative if other disciplines than OB-GYN specialists were included in the makeup of the Committee?

As long as I am being critical the grammar and spelling of the report could well tolerate some editorial scrutinizing—e.g., how does a patient "receive" a Hysterectomy and Nisentil. Thank you.

Donald W. Stein, MD
Boulder, Colorado

Editor's Comment: The Maternal Mortality Committee is a subcommittee of a committee of the Council on Public Health of the Colorado Medical Society. Dr. Stein's recommendation that disciplines other than obstetrics and gynecology be included is referred to the CMS Board. The editor agrees that the report should be edited prior to publication in the ***Rocky Mountain Medical Journal.***

To the Editor:

Thank you so much for dedicating the cover of your *Rocky Mountain Medical Journal* to the American Indian costume exhibition, *Robes of White Shell and Sunrise.* The exhibition is an extremely fine one and we, of course, are anxious to have as many people know about and have a chance to enjoy it.

May I also express my thanks for all the other attention you have given the Museum over the past year. In my months here I have come to realize even more fully how great a public resource for enjoyment the Museum is, and how important it is to spread the word as widely as possible. Doctors, of course, have been among the most active and knowledgeable in the arts, but I am also sure that your *Journal* is widely read by patients as well.

Thomas N. Maytham
Director, Denver Art Museum
Denver

To the Editor:

Congratulations on your editorial "Shameful Exposure," in your November issue.

I am a surgeon. I have had a vague sensation of discomfort and sympathy for the patient who has had all the statistical basis for her prognosis explained in minute detail as a result of news medium stories—rather than a mercifully short and more emotionally effective explanation by her medical advisor. The effect on the rest of the population is equally disturbing, although for a different reason. I am glad you so effectively stated the case.

May I have permission to reprint your editorial in our journal with, of course, credit to the *Rocky Mountain Medical Journal*?

Frank B. Ramsey, M.D.
Editor, *The Journal of the*
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in Brief

A summary of AMA, medical & health news

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The AMA and other professional organizations will cooperate in the development of a major real estate complex on four blocks adjoining the AMA Headquarters. Long-range plans include a professional association campus and a center for continuing education. The campus will be built on land owned by the AMA and the AMA Members Retirement Plan, but neither will own any buildings in the complex. The land will be leased to the Urban Investment and Development Co. of Chicago, which will plan and develop the property. The first construction is planned for mid-1975 and will probably continue for ten years.

$30 million will be awarded by the Robert Wood Johnson Foundation to approximately 60 community hospitals and their medical staffs to assist in establishing primary care group practices over the next five years. About 900 community hospitals have received invitations to submit proposals. The awards will be announced in 1976. Every state is expected to have at least one program in which groups of three or more full-time physicians offer round-the-clock primary care for up to 15,000 people each.

Fifty national non-governmental organizations will establish a National Commission on Confidentiality of and Access to Health Care Records. The commission will make studies and recommendations, and will encourage member organizations to seek legislative action. The commission grew out of a conference on the subject of confidentiality, sponsored by the AMA and other groups. There, a study group recommended that all information used by PSROs be considered confidential and that PSROs be exempted from state laws requiring the reporting of certain health data.

There are eight fewer acupuncture clinics in the Washington, D.C. area today than there were nine months ago. Then, a dozen clinics employed about 50 Oriental acupuncturists, and now there are only four clinics and a total of eight acupuncturists. Patient loads have decreased from about 200 a day to about 25. The demise of the clinics in the D.C. area is the result of a survey of them by the Medical Society of District of Columbia, a call for speedy improvements, mounting public reaction, and the recommendation from the AMA's delegation to China that acupuncture be allowed in the U.S. only as an experimental treatment.

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WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**
Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)
Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development) Embryotoxicity has also been noted in animals treated early in pregnancy
Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)
All tetracyclines form a stable calcium complex in any bone-forming tissue A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued
Tetracyclines are present in milk of lactating women taking tetracyclines.
To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug The anti-anabolic action of tetracyclines may increase BUN While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.
Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema
PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy
In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.
Tetracyclines have been shown to depress plasma prothrombin activity, patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage
In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).
Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.
ADVERSE REACTIONS: **Gastrointestinal** (oral and parenteral forms) anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region
Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**)
Renal toxicity: rise in BUN apparently dose related (See **WARNINGS**).
Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.
Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.
Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.
Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands, no abnormalities of thyroid function studies are known to occur
USUAL DOSAGE: **Adults** – 600 mg daily, divided into two or four equally spaced doses. More severe infections: an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours Gonorrhea In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule 900 mg initially, followed by 300 mg q i d for a total of 5.4 grams
For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given Close follow-up, including laboratory tests, is recommended
Eaton Agent pneumonia 900 mg daily for six days.
Children – 3 to 6 mg/lb/day divided into two to four equally spaced doses.
Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided
Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated Food and some dairy products also interfere Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding
In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.
In streptococcal infections, a therapeutic dose should be given for at least 10 days.
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***Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows: "Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.
Warnings: *Usage in Pregnancy*—Use in women of childbearing potential only when potential benefits outweigh possible risks.
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Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-four patients, it was not possible to state that the dysfunction was or was not drug induced.
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References: 1. Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 1955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, F.N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: New Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboratories, Inc.

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We've Come a Long Way, Baby!

THE BOARD OF TRUSTEES of the American Medical Association has proposed that advertising in all AMA publications be discontinued. Their reason is that the majority of advertising in these thirteen publications is by pharmaceutical houses, and the AMA has been accused of conflict of interest. That the accusation is absurd is not enough. That the Board of Trustees yields to this charge is unbelievable. The government, spurred on by self-appointed consumer advocates, persists in the attempt to control medicine and the drug industry. That the official representatives of medicine would capitulate to demands based upon the presumption that physicians are either stupid or crooked vividly points up how scared we run.

Another issue to which we seem to react with either fear or ignorance is government supervised recertification. This proposal is another attack on medicine by the politicians in their exploitation of the political potentials of health care. In turn, physicians are caught up by a high sounding phrase and a logical-sounding concept. Because of our heritage of interest in progress in our science, and because of our basic confidence that we are doing a good job, to be recertified at varying intervals does not sound unreasonable. But—when we seriously think about this proposal, it is obvious that government supervised recertification is not necessary, will not work, and is a malignant danger to us and to our patients.

Since the dawn of medicine physicians have been individually and collectively reassessing their knowledge because assessment of result is the measure of effectiveness of treatment. Continuing education has always been part of practicing medicine. Our profession has more journals and scientific publications than all the rest put together. It has always been recognized that the physician spends more of his extra time in learning than any other profession or trade. Over the past twenty years continuing education programs at all levels have been burgeoning as physicians voluntarily attempt to stay abreast of the expansion in medical knowledge. More recently, self-assessment programs of various medical organizations have been introduced, and the Recognition Award of the American Medical Association has been promoted. It is incomprehensible that of all professions *we* should be singled out for recertification.

From a practical point of view universal government supervised recertification is impossible. A written examination can evaluate only certain types of knowledge, not total knowledge. Moreover there is no direct relation between knowledge and performance. By an examination there is no way to evaluate motivation or dedication. There is no way to test for ability in even the simple skills. There is no way to assess experience or judgment. Moreover, the bureaucracy that would be required to recertify on the basis of this limited evaluation of a physician's competence would rival the Pentagon in size, and it would eventually have total control of health care in America. And this proposal becomes even more absurd because we already have in operation an excellent method of *continuous* evaluation of the competence of most physicians—the hospital staff. The hospital staff through its committees, meetings, and programs is a workable and inexpensive mechanism for evaluating total performance.

We in medicine actually have a powerful position. We are the only persons who can take care of the medical needs of the nation. We are providing the best health care in the world. We are the most educated, most dedicated, most self-disciplined profession in America. Yet our once proud, confident, and noble profession now moves with fear and operates with self-incrimination. We've come a long way, Baby.

Utah Withdrawal

With regret we report that the Utah State Medical Association has withdrawn from the *Rocky Mountain Medical Journal.* The Board of Trustees of that association made their decision for compelling financial reasons. Because of increased costs of printing, paper, and mailing it was necessary to increase the yearly subscription rate of the *Journal* from $3.50 to $6.00. The houses of delegates of our other five states approved this increase and absorbed it into their budgets. It was the opinion of some of the delegates of one of these states that the Rocky Mountain Directory of Physicians alone was worth the subscription price of the *Journal.*

The principal reason that we do not agree with the action of the Utah Board is that in our opinion over the years the small amount of the dues of the member for his *Journal* subscription has produced proportionately more dividends than huge sums spent for other things, particularly activities to stave off socialized medicine. We certainly were, and are, in full support of these latter expenditures, but the fact is that *in the relentless effort of government to take over medical practice, the scientific power base of medicine is our strongest asset.* Our basic strength is that we are scientists and doctors. When we compete with stock brokers, investment bankers, and others in commercial enterprise, or when we deal with politicians, we are at a disadvantage by training and heritage. Our major strength in the social scheme is that we are experts in medical care. Every time we abandoned a scientific or professional activity for political expediency we lose prestige and power.

We regret that Utah has withdrawn from a thirty-seven-year association with the *Rocky Mountain Medical Journal.* We are sad that they have dented the camaraderie among our Rocky Mountain states that association through the *Journal* helps to provide. We sincerely wish the Utah State Medical Association success. We invite them, someday, to reconsider their decision.

The Fifth annual Mount Airy Foundation Gold Medal seminar, luncheon and banquet will be held on Saturday, March 1, in the Brown Palace West ballroom, Denver.

The morning session from 9:30 to 11:45 deals with The Impossible Years: Adolescents and Parents in a Changing World, with Albert J. Solnit, MD, speaking on "Identity Development in Adolescence: How to Be Me," and Elwyn James Anthony, MD, on "Getting The Kids You Deserve."

Sidney L. Werkman, MD, will speak on "Early Adolescence: The New Dawn," and John Janeway Conger, Ph.D., speaks on "Where Have All the Flowers Gone?" in the afternoon seminar which goes from 2 p.m. through 4:45.

Both seminars are open to the public without charge.

Maurice B. Mitchell, chancellor of the University of Denver, will speak on "Desegregation or Integration?" at the luncheon at 12:15 p.m., for which there is a charge of $6.00.

The award banquet is at 7:30 p.m. in the ballroom. At this occasion Albert J. Solnit, MD, will be given the 1975 Mount Airy Gold Medal, following which he will make an address on "The Adolescent and His Family."

Treatment of adult acute non-lymphocytic leukemia*

Jan L. Gray, MD, and
William A. Robinson, MD, PhD, Denver

Of twenty-one adults with acute non-lymphocytic leukemia, a remission in eight and partial remission in three was obtained with a chemotherapeutic regimen of cytosine arabinoside and 6-thioguanine.

Acute leukemia has been considered a rapidly fatal disease. However, results of chemotherapy of childhood acute lymphocytic leukemia have greatly improved, with both a high initial complete remission rate and an increasing number of long term survivals, some of whom may be cured.[1] Results of therapy in acute non-lymphocytic leukemia, particularly in adults, have not been nearly as impressive.

Without therapy the median survival of patients with acute leukemia is about three months.[1] The use of 6-mercaptopurine proved that drug induced remissions in acute leukemia are possible,[2] but the median rate of 10 per cent in acute non-lymphocytic leukemia was disappointingly low.[3,4] Combinations of effective chemotherapeutic agents such as vincristine, 6-mercaptopurine, prednisone, and often methotrexate resulted in a significant improvement in complete remission rate to about 30 per cent.[5] Recently with daunomycin[6] or with cytosine arabinoside and 6-thioguanine[7-9] complete remission rates approaching 50 per cent have been reported.

From July, 1971 to the present, adults with acute non-lymphocytic leukemia have been treated at the University of Colorado Medical Center with a combination of cytosine arabinoside and 6-thioguanine administered at twelve hour intervals. It is the purpose of this report to present the rationale and results of this program of chemotherapy.

Materials and Methods

All adults seen at the University of Colorado Medical Center with acute non-lymphocytic leukemia between May, 1971 and April, 1973, who were treated with a combination of cytosine arabinoside and 6-thioguanine given at twelve-hour intervals are included in this report. Patients in the blastic crisis of chronic granulocytic leukemia or polycythemia vera, or with erythro-leukemia were not included in this study. Two patients who died on the day of referral before the initiation of chemotherapy were excluded. Twenty-one patients, sixteen males and five females, ranging in age from 18 to 69 years with bone marrow biopsies diagnostic of acute non-lymphocytic leukemia were treated.

The first three patients were treated with cytosine arabinoside 3 mg/Kg intravenous push and 6-thioguanine 1.25 mg/Kg orally every 12 hours until marrow depletion proven by marrow biopsy occurred. Subsequent patients were treated with nine-day courses of cytosine arabinoside given by rapid intravenous injection and 6-thioguanine given orally as follows: Ara C, 6 mg/Kg, i.v. every 12 hours for 6 doses, then 3 mg/Kg i.v. every 12 hours for 6 doses, then 1.5 mg/Kg i.v. every 12 hours for 6 doses, and 6-thioguanine 1.25 mg/Kg orally every 12 hours for nine days. A rest period of 20 days followed with a repeat bone marrow biopsy being done 16 to 19

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*From the Division of Hematology, Department of Medicine, University of Colorado Medical School, Denver. Supported by grants from the Monfort Hematology Fund, National Institutes of Health, National Cancer Institute (1R01CA11305-04 and CA05058-10), and by the American Cancer Society Grant #ET-4B, and by grant (RR-51) from the General Clinical Research Centers Program of the Division of Research Resources, National Institutes of Health. Address Communications to: William A. Robinson, MD, PhD.

days after completion of this course of chemotherapy. If leukemic infiltration of the marrow persisted, another nine-day course of combination chemotherapy was undertaken. If the marrow biopsy showed a remission, the patient was placed into a maintenance phase of chemotherapy consisting of Ara C 3 mg/Kg i.v. every 12 hours and 6-thioguanine 1.25 mg/Kg orally every 12 hours for 4 days. Maintenance therapy was repeated at monthly intervals. All patients received allopurinol and most received blood and/or platelet transfusions. Antibiotics were administered as needed.

Results

Seven of eleven patients under the age of 50 years with a range of 18 to 47 years went into complete remission as a result of chemotherapy (Table 1). Complete remission was defined as H-1 hemogram, M-1 marrow, P-1 physical findings and S-1 symptomatology using the criteria established by the Midwest Cooperative Chemotherapy Study Group.[10] One patient achieved a partial remission. Three patients, all of whom survived long enough to receive an adequate course of therapy, failed to go into remission.

TABLE 1

RESULTS OF TREATMENT IN ELEVEN ADULTS UNDER AGE FIFTY

	Number	Per Cent	Medial Remission Duration	Medial Survival Time
Complete Remission	7	64	9+ months	11+ months
Partial Remission	1	9	3 months	23 months
No Response	3	27		4 months

Results of chemotherapy in ten patients ranging in age from 54 to 69 years were much poorer, there being one complete and two partial remissions (Table 2). Six of the seven therapeutic failures did not survive the induction phase of therapy, dying within 20 days of initiation of chemotherapy, precluding the possibility of a remission since survival for at least three weeks is necessary to achieve remission.

Of the eight patients in this series of twenty-one who achieved complete remission, seven required only one nine-day course of therapy. The other patient went into complete remission after two courses of combination chemotherapy.

Except for occasional nausea and vomiting, drug toxicity was primarily that of bone marrow depression. All except two patients developed significant neutropenia during the course of therapy, most having white blood counts less than 1,500 mm^3. In two patients the lowest white blood counts were 10,000 mm^3 and 12,000 mm^3, and neither went into remission. The platelet count in all patients fell to less than 15,000 mm^3 during the course of therapy. The initial platelet and white blood count were of no value in predicting results of chemotherapy. The one patient in this series with an initial white blood count greater than 100,000 mm^3 went into a complete remission. Hemorrhages and infections were the major causes of morbidity and mortality during therapy.

TABLE 2

RESULTS OF TREATMENT IN TEN ADULTS OVER AGE FIFTY

	Number	Per Cent	Medial Remission Duration	Medial Survival Time
Complete Remission	1	10	6+ months	7+ months
Partial Remission	2	20	5 months	8 months
No Response	7	70		3 months

Discussion

Although long term results have been disappointing in adult acute non-lymphocytic leukemia, there has been an improvement in the complete remission rate with treatment by the newer chemotherapeutic agents. One of the better combinations has been cytosine arabinoside and 6-thioguanine.[7,8] These agents are cycle dependent interfering with the DNA synthesis phase of the cell generation cycle. Use of these drugs in this protocol was designed to take advantage of experimental cell kinetic studies.

Regardless of etiology, it is generally believed that acute leukemia represents an uncontrolled proliferation of an immature abnormal clone of cells which coexists with normal hematopoietic stem cells. Unfortunately, agents effective against the cells of acute non-lymphocytic leukemia also destroy normal hematopoietic tissue. Experimentally, however, there is a difference in cell kinetics between normal and leukemic cells,[11,12] and it should be theoretically possible to utilize these differences in the chemotherapy of acute leukemia to preferentially destroy leukemic cells.[13]

In the process of cell division, cells pass through several phases of activity. After mitosis (M) there is a resting phase (G_1) followed by a DNA synthesis phase (S), in turn followed by another resting phase (G_2) which precedes mitosis. The generation time is the length of time it takes for a cell to complete this cycle. In acute leukemia, some leukemic cells are apparently in a prolonged G_1 phase, sometimes called G_0, lasting for days. These resting cells are thought to be the reservoir of leukemic stem cells which are relatively insensitive to any type of therapy. Experimental studies of cell kinetics indicate that the various phases of cell generation are prolonged in time over those of normal hematopoietic cells (Table 3).[11-13]

TABLE 3

MITOTIC CYCLE TIME OF NORMAL AND LEUKEMIC CELLS IN HOURS

	G_1	S	G_2	M	Generation Time
Normal	4	6-24	2	0.5	24
Leukemia	10->200	16-24	3	1	40-100

Kinetic studies indicate that if the marrow is depleted of both normal and leukemic cells to the same degree, normal marrow should return first because of its shorter generation time. This therapeutic strategy presupposes that enough normal stem cells survive chemotherapy to repopulate the marrow and that the patient survives the necessary severe marrow hypoplasia. Using results of cell kinetic studies it is theoretically possible to design a chemotherapy program which improves the survival advantage of normal over leukemic stem cells. Results of kinetic studies form the basis for administering the cycle active agents cytosine arabinoside and 6-thioguanine at twelve-hour intervals.

At the time of diagnosis of acute leukemia it is thought that most proliferating cells are leukemic whereas most normal stem cells are in a prolonged resting (G_1 or G_0) phase.[14] If this is true it would be desirable to initially administer high doses of cycle dependent chemotherapeutic agents attempting to destroy as much leukemic tissue as possible while normal stem cells are relatively protected from the action of the drugs. As the marrow becomes depleted, stem cells presumably both normal and leukemic, enter a proliferative state. It is then reasonable to decrease the dosage of cycle dependent drugs to preserve some normal hematopoietic tissue.

The rationale for an every 12 hour pulse therapy regimen is based on the DNA synthesis time (S phase) of proliferating cells. If leukemic cells are in the S phase for 16 to 24 hours, S phase dependent drugs given at 12 hour intervals should be effective against the majority of proliferating leukemic cells. Conversely if normal cells synthesize DNA for 6 to 24 hours, some normal hematopoietic cells should complete the S phase between 12 hour dosages of chemotherapy and therefore avoid destruction. A twelve-hour intermittent schedule of S phase active drugs should therefore confer a survival advantage on normal hematopoietic cells.

There is some evidence that intermittent administration of cycle dependent chemotherapeutic agents leads to a synchronization of leukemic cells in S phase.[15-17] Furthermore, this effect does not seem to occur with normal myeloid precursors.[16] This effect should increase the number of leukemic cells susceptible to S phase drugs without changing the susceptibility of normal myeloid cells.

The obvious disadvantage of cycle active chemotherapeutic agents is that they are ineffective against resting (G_1 or G_0) cells, normal or leukemic, making it impossible to eradicate the leukemic cell population. However, agents effective against resting cells destroy both leukemic and normal cells conferring no particular advantage to normal cells and therefore no advantage to the patient. Means of therapy other than logarithmic cell kill by drugs will need to be developed before cure of acute nonlymphocytic leukemia becomes a realistic possibility.

Results of this chemotherapeutic protocol lend support to the theoretical advantage of intermittent twelve-hour administration of the S phase active drugs cytosine arabinoside and 6-thioguanine in younger adults with acute nonlymphocytic leukemia. Unfortunately results continue to be dismal for the older patient. The difference in results in chemotherapy between younger and older patients is partially explained by the ability to tolerate the hypoplastic marrow phase of therapy. Most of the older patients who failed to achieve remission died during the hypoplastic phase of induction therapy from bleeding or infection, whereas most younger patients survived the hypoplastic phase long enough to at least have the possibility of a remission from leukemia.

The current approach to adult acute nonlymphocytic leukemia at this medical center is aggressive chemotherapy with cytosine arabinoside and 6-thioguanine given at twelve-hour intervals for younger patients since they have a good chance for complete remission with a prolongation of survival. However, for older patients it seems more appropriate to use supportive therapy until significant complications of leukemia occur at which time chemotherapy can be instituted. Possibly lesser doses of chemotherapeutic agents should be used in older patients because of their poor ability to tolerate severe bone marrow hypoplasia.

Summary

Twenty-one patients with adult acute nonlymphocytic leukemia were treated with a combination of cytosine arabinoside and 6-thioguanine given every 12 hours for nine-day courses. Seven of eleven patients under the age of 50 and one of ten patients over the age of 50 obtained complete remission. Three patients achieved partial remission. The major reason for the poorer results in older patients was apparently their inability to tolerate the hypoplastic phase of induction chemotherapy. Six of the ten older patients died within three weeks of initiation of chemotherapy. The rationale and results of this chemotherapy protocol are discussed. •

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Delayed hypersensitivity reaction at metastatic tumor sites

Robert E. Gerner, MD*, George E. Moore, MD, and
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Delayed hypersensitivity reactions occurred **in vivo** ***at distant metastatic tumor sites following active specific immunotherapy by intradermal inoculations of cultured irradiated human melanoma cells.***

The DEMONSTRATION OF tumor associated antigens capable of inducing selective cell-mediated cytotoxicity confined to malignant cells has focused increased attention on the possibilities of immunologic intervention in the clinical management of cancer.[1-4]

Various clinical studies of immunization with cultured tumor cell preparations injected subcutaneously in patients with far advanced neoplasia and *unknown immunocompetence* have been reported by us previously.[5,6] Although these procedures had no significant effect on the clinical course of the neoplasia in a majority of the patients, these studies demonstrated the safety of the inoculations and provided some dramatic instances of tumor regression. Subsequently, the existence of cellular immunity in solid cell neoplasia was suggested by the demonstration of cutaneous hypersensitivity reactions to autologous extracts of these tumors.[7,8] These observations prompted a preliminary clinical study as an attempt to augment cellular tumor immunity by intradermal immunization (hypersensitivity) with cultured homologous tumor cells in *immunocompetent* patients. The study was designed and performed to obtain information relevant to methodology and toxicity of these agents, and for supplemental data, related to possible alterations of cellular immunity.

This report summarizes our observations of the effects of this intradermal immunization procedure in twelve immunocompetent patients. The striking appearance of delayed hypersensitivity reaction at metastatic tumor sites was observed in one of the patients. A summary of this case history is presented.

Methods

This study protocol was approved by the Institute's Clinical Investigative Committee, and only volunteer immunologically competent patients with full understanding of the procedure were studied. Immunologic competence was assessed by cutaneous reactions to intradermally injected microbial antigens and the induction of sensitivity to topically applied sensitizing agents as outlined below.

A. Microbial Skin Test Antigens
   1. Tuberculin—second strength purified protein derivative of tuberculin 0.1 cc (250 U.S. Units)—Connaught Medical Research Laboratories.
   2. Mumps, 0.1 cc of skin test antigen. Eli Lilly and Company.
   3. Strepto-Kinase-Streptodornase (Varidase), 100 units/ml, 0.1 cc used. Lederle Lab Division.
   4. Dermatophytin and Dermatophytin "O". 1:10 dilution, diluted 1:1000 and 0.1 cc used. Hollister-Stier Laboratories.
   5. Coccidioidin, 1:100, 0.1 cc used. Cutler Laboratories.
   6. Histoplasmin, 1 cc diluent per vial and of this 0.1 cc used. Parke-Davis.
   7. Control, 0.1 cc saline.

B. Topical Sensitizing Agents (Neo-Antigens):
   1. Dinitrochlorobenzene (DNCB) Crystalline from K & K Laboratories. Used as 0.1% concentration in acid mantle cream.
   2. 2, 3, 5-Tri-Ethylene-Imino-1, 4-Benzoquinone (Trenimon) Powder from Farben Fabriken Bayer/AB. Used as 0.01% topical ointment in petrolatum.
   3. AB-132 powder from Stark Associates. Used as topical cream 2% in Aquaphor.

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TABLE 1

CELL INJECTION SCHEDULE

Day	No. Cells	Day	No. Cells
1	25×10^6	11	100×10^6
3	50×10^6	13	100×10^6
5	75×10^6	15	200×10^6
7	100×10^6	23	200×10^6
9	100×10^6	Then 200×10^6 q 3-4 wks.	

These neo-antigens were applied individually, to a 1 to 2 cm area of skin on the upper arm under an occlusive dressing and reapplied to the same area every three days, until induction of sensitivity was evident to one or more of the agents, which usually required two to four weeks. Cutaneous reactions to the microbial antigens were recorded at 24, 48, and 72 hours, and a positive skin test was defined as an area of erythema and induration greater than 10 mm in diameter. Induction of *de novo* sensitivity to the neo-antigens was defined as an area of induration and erythema at the application site of the sensitizing agent. This induced *de novo* sensitivity could be readily demonstrated (within 8 to 10 hours) following challenge with the same neo-antigen at remote skin sites. Patients were considered immunocompetent if they demonstrated recall (positive skin test) to two or more of the microbial skin test antigens, and the capacity to develop *de novo* sensitivity to one or more of the neo-antigens.

Tumor cell preparations used for inoculations were from established and maintained human cell lines of a malignant melanoma, RPMI #3236, and an osteogenic sarcoma, RPMI #41. Recipient patients were inoculated with tumor cells of their respective tumor type. These cell lines were grown in RPMI media 1640 supplemented with ten per cent fetal calf serum. Stationary cultures were harvested by scraping the cells from the glass surface with a rubber spatula and washed five times in phosphate-buffered saline to eliminate residual fetal calf serum. Cell counts were made in the presence of one per cent trypan blue stain for cell viability. The sterility of all tumor cell preparations was assessed and they were irradiated with 5000 Rads prior to inoculations. The tumor cells were administered intradermally in the anterior thighs of intact lymph node bearing extremities according to the treatment schedule outlined in Table 1. These sites were observed closely for evidence of tumor growth; none was seen.

Serial examinations of the total and differential peripheral white blood counts were performed. Blood sera were obtained and stored in the vapor of liquid nitrogen for studies of possible humoral antibody production and for the detection of fetal calf serum antibodies.

Results

In this study group of twelve immunocompetent patients, there were five with a histologic diagnosis of osteogenic sarcoma and seven with malignant melanoma. Seven patients were entered into the study immediately following "curative" surgical procedures with confirmed pathologic Stage II disease and thus they were classified as "high risk" for recurrence. The treatment period was five months in three patients, six months in five patients, seven months in two patients, 27 months in one patient, and 42 months in one patient.

All twelve patients developed marked cutaneous reactions at each subsequent cell injection site following the initial three to four interval cell injections. The pattern of these cutaneous reactions was uniform and commenced in eight to ten hours with local pruritus, induration, and a 5 to 10 cm area of erythema. These reactions reached a peak in 72 to 84 hours and slowly subsided during the next several days. A fever of 101° to 102° F and/or a flu-like syndrome were observed in seven of the twelve patients.

One patient developed the equivalent of delayed hypersensitivity reactions at clinically undetected metastatic tumor sites.

CASE REPORT

Case 1: A 43-year-old white male had a malignant melanoma excised from his back in 1956. His first recurrence presented as metastasis in a 3 x 3 cm node in the left axilla removed by a left axillary node dissection in May, 1969. He had no clinical or laboratory evidence of other metastasis.

Intradermal inoculations of cultured melanoma cells were initiated on May 27, 1969. Local cutaneous reactions of pruritus, induration, and a 5 to 10 cm area of erythema commenced at each new inoculation site within 8 to 10 hours. Simultaneously, systemic reactions described as "flu-like", consisting of a generalized ache and a temperature of 101° to 102° F were noted. On the 28th treatment day, 8 to 10 hours after the ninth interval inoculations were administered, he developed, in addition to the local and systemic reactions, a "bee sting" in the area of his right elbow (Fig. 1). While rubbing this pruritic, red, indurated area, he detected a subcutaneous nodule measuring less than 1 cm in diameter. Unaware of the possible significance

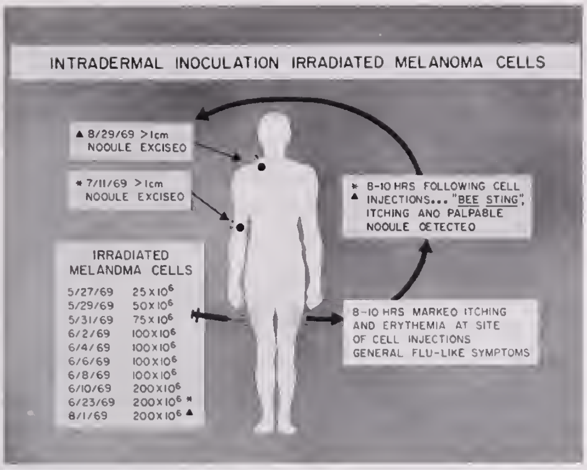
INTRADERMAL INOCULATION IRRADIATED MELANOMA CELLS
▲ 8/29/69 >1cm NODULE EXCISED
* 7/11/69 >1cm NODULE EXCISED
* ▲ 8-10 HRS FOLLOWING CELL INJECTIONS... "BEE STING", ITCHING AND PALPABLE NODULE DETECTED
IRRADIATED MELANOMA CELLS
5/27/69 25 x 10⁶
5/29/69 50 x 10⁶
5/31/69 75 x 10⁶
6/2/69 100 x 10⁶
6/4/69 100 x 10⁶
6/6/69 100 x 10⁶
6/8/69 100 x 10⁶
6/10/69 200 x 10⁶
6/23/69 200 x 10⁶ *
8/1/69 200 x 10⁶ ▲
8-10 HRS MARKED ITCHING AND ERYTHEMIA AT SITE OF CELL INJECTIONS GENERAL FLU-LIKE SYMPTOMS

Fig. 1. Outline of the treatment course of the patient with delayed hypersensitivity reactions occurring at clinically undetected metastatic tumor sites, Case 1. Note the local reactions of erythema and induration following each intradermal inoculation of the tumor cells in the thighs and in addition, on two separate occasions (6/23/69 and 8/1/69), the delayed hypersensitivity reactions occurring at clinically undetected metastatic tumor nodules of the right elbow and shoulder.

of this episode, he did not inform his physician of the unusual finding for several days. A delay of 18 days elapsed before the nodule was excised. Pathologic study showed a tumor nodule with a necrotic center and abundant lymphoid cells infiltrating a peripheral rim of tumor cells (Fig. 2). Thirty-nine days later, he received his tenth intradermal inoculations of 200 x 10^6 irradiated cultured melanoma cells in both thighs, and the same phenomenon of localized pruritus, pain, erythema and induration occurred again 8 to 10 hours later in the upper portion of his right arm. Again, an undetected subcutaneous nodule less than 1 cm in diameter was found. This nodule was excised 28 days later at his next clinic appointment and pathologic examination demonstrated a tumor nodule 0.5 cm in diameter with central coagulation necrosis and abundant lymphoid cells present in a capsule surrounding the nodule.

Subsequently, while on treatment, he developed an enlarged right axillary node which proved to contain no tumor on microscopic examination following right axillary node dissection. During the next four months while on treatment, he presented with unexplained anemia presumed to be secondary to metastatic melanoma lesions in the gastrointestinal tract even though radiographic studies of the small bowel were interpreted as negative, In November, 1969 he developed small bowel obstruction which proved at operation to be intussusception secondary to a metastatic lesion in the small bowel. There were multiple metastatic lesions in the small bowel. He was started on chemotherapy with dimethyl triazeno imidazole carboxamide without effect and he died on March 30, 1970.

In this study, two other patients may have benefited from the cell injections, but no claim of therapeutic benefit can be made. Their brief case histories are included to demonstrate the pattern of immunotherapy that is being used.

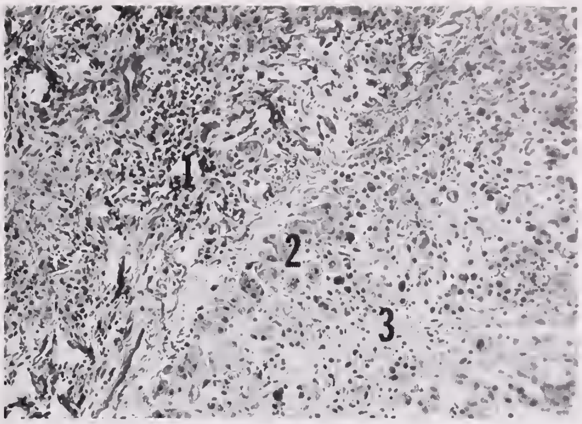

Fig. 2. Pathohistologic features of the distant metastatic nodule which was excised on 7/11/69 as shown in Fig. 1. At site 1 there is lymphoid cell infiltration surrounding a rim of a few viable tumor cells, and at 2 and 3 there are areas of tumor cell necrosis within the capsule of the tumor nodule.

Case 2. A 48-year-old white male underwent local excision of a malignant melanoma of the left anterior chest wall in September, 1967. His first recurrence presented as a metastatic node, measuring 6 cm in diameter, in the left axilla which was removed by a left axillary node dissection in May, 1969. During the post-operative course, intradermal inoculations of cultured melanoma cells were initiated. Eight to ten hours following each inoculation, marked local reactions consisting of pruritus, erythema, and induration developed at each new vaccination site. Cell inoculations were given every three to four weeks from June 1969 through July 1973, at which time all therapy was discontinued. A total of eight grams of cultured cells were administered during this interval. He has remained clinically free of either local or distant recurrent disease with no further therapy for over 18 months.

Case 3. A 10-year-old boy underwent disarticulation of the left leg at the knee joint in June of 1968 for osteogenic sarcoma of the distal tibia. He was entered into the study following wedge excision of a metastasis in the upper lobe of the right lung in February of 1969. Subsequently, while on therapy, a single metastasis 1.5 cm in diameter was excised from the left upper lobe of lung in January, 1970 and a second solitary metastasis of left lower lobe was excised in May, 1972. During this interval five grams of cultured osteogenic tumor cells were administered and he has remained free of further metastatic disease without treatment for two years and seven months.

In the remaining nine of the twelve patients, this form of treatment was of no apparent benefit since there was a relentless progression of their disease.

Study of the peripheral blood counts of the twelve patients is summarized in three groups as listed below. These figures represent an average of two counts prior to the immune therapy, A, and an average of all counts during immune therapy, B.

Group 1 (Four Patients)

A. Normal WBC, normal differential
B. Normal WBC, shift of 50% or more in lymphocytes, basophiles and monocytes

Group 2 (Three Patients)

A. Normal WBC, lymphocytosis and/or monocytosis and basophiles
B. No Change

Group 3 (Five Patients)

A. Normal WBC, normal differential
B. No change

This series of patients is too small to evaluate changes in the peripheral blood counts in relation to possible alterations of immunity. Case 1 of the three patients presented in the brief histories above was in Group 2, Case 2 was in Group 3 and Case 3 was in Group 1.

Discussion

The clinical and histologic data presented in the first case report indicate that delayed hypersensitivity reaction occurred *in vivo* at distant metastatic tumor sites following active *specific* immunotherapy by intradermal immunization with homologous melanoma cells. No published report of a similar phenomenon was found in the literature.

Complete regression of superficial cutaneous neoplasms has occurred following the use of two related, active *non-specific* immunotherapy procedures, namely: (1) induction of *de novo* sensitivity to a topical sensitizing agent such as DNCB, which is then applied directly to superficial lesions resulting in localized delayed hypersensitivity reactions[9], and (2) intratumor inoculation of BCG (bacillus Calmette-Guerin) which has produced complete regression of many of the inoculated lesions, but only a few adjacent untreated lesions.[10,11]

Both of these procedures are limited to small superficial lesions, and, to our knowledge, there are no published reports indicating complete regression of measurable remote distant metastatic lesions following either form of therapy. Again the destruction of individual lesions after the injection of BCG may be important from a scientific viewpoint, but it has no clinical significance. However, the goal which cannot be lost sight of, it should be emphasized, is the destruction of distant metastases, often of considerable size.

In this report, in one patient delayed hypersensitivity reactions occurred at a distant metastatic lesion on two separate occasions. The lesions were excised for histologic study and both were surrounded by an abundant mononuclear cell infiltration and evidence of tumor necrosis. It is also evident that after a period of time, remote disease sites were not affected by this phenomenon of delayed hypersensitivity. There may be several possible causes for this failure: (1) there was only partial cross reactivity between "antigens" of the cultured tumor cells and those tumor cells of the host; (2) the "tumor-antigen" of the cultured cells may have been extremely weak with minimal stimulation of cell-mediated immunity; (3) there were differences in "tumor antigens" of tumor cells in different metastatic tumor sites; and finally (4) repeated cell injections may have produced an immunodepressor or blocking effect rather than immunostimulator or killer effect. Further studies to identify common cross reacting tumor antigens are needed before usefulness of cultured cells can be expected. •

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Carcinoembryonic antigen (CEA) assay

In diagnosis and management of cancer

P. F. Bray, MD, J. T. Wu, PhD, and A. C. Madsen,
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SEARCH FOR AN ACCURATE comprehensive diagnostic tool for cancer continues. During the past ten years isolation of the so-called carcinoembryonic antigen, CEA, from colon carcinoma and fetal gut tissues led to the development of a radioimmunoassay for nanogram quantities of this substance in human plasma.[1-3] Much time and effort has been invested in modifications of the method and in the collection of data to establish normal values so that the assay could be evaluated in patients with all types of malignant and nonmalignant disease.

The purpose of this short communication is (1) to describe the method of sample collection, storage and assay and (2) to summarize the findings in a series of patients with various malignant disease, emphasizing the test's value and limitations for both diagnosis and monitoring of therapies. The study was done in conjunction with Hoffmann-LaRoche, Inc. who have marketed the assay in "kit" form as CEA-Roche.

The CEA radioimmunoassay has recently entered general laboratory usage after extensive collaborative testing. When the determination is used in conjunction with conventional technics in patients suspected of having malignancies, it has been found helpful both for diagnosis and for monitoring the patient's response to therapy. Highest CEA values are seen in patients with colorectal, pulmonary, breast, and pancreatic carcinoma. Plasma CEA values fall after successful therapy whereas rising values worsen the prognosis and may reflect metastatic disease. When high levels are encountered the assay should be repeated using dilutions of the sample.[4] The assay is *not* a reliable screening test because of a variable per cent of "false negative" studies in patients with proven malignancies. Also, elevated values ("false positives") are encountered in some clinically active nonmalignant diseases and in some malignancies which are not carcinomatous. Ninety-seven per cent of healthy nonsmoking controls have CEA values between 0 and 2.5 ng/ml.

Method

Plasma specimens are obtained as follows:

Five to ten milliliters of blood are collected in a lavender-topped Vacutainer† tube containing liquid EDTA. The tube is inverted gently several times to insure proper mixture. The sample is then centrifuged at 1,000 x g for 30 minutes either within 6 hours if the specimen is left at room temperature, or within 12 hours if the specimen is refrigerated at 4°C. The supernatant is promptly withdrawn with a disposable Pasteur pipette. If the test is run in one's own hospital laboratory, the plasma sample is refrigerated at 4°C. If the plasma sample is sent to an outside laboratory, it should be shipped promptly. If exposure to excessive heat is anticipated, the sample should be shipped to arrive

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† Becton, Dickinson & Co.

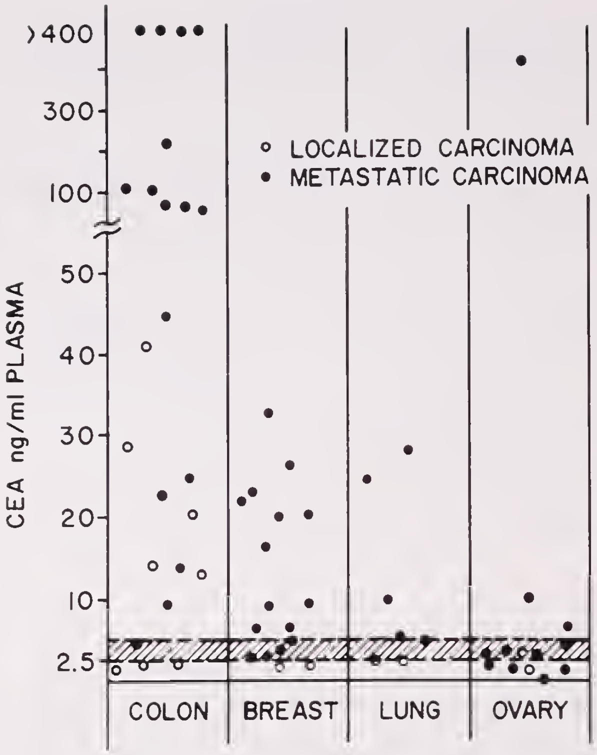

Fig. 1. CEA determinations in patients who may be expected to exhibit elevated levels (pancreatic carcinoma is not represented because it failed to appear in this small sample). The open circles depict determinations from patients with apparently localized disease; closed circles represent those from patients with metastatic malignancy. A single value in the "gray zone" (2.5-5.0 ng/ml) may or may not be abnormal for that patient.

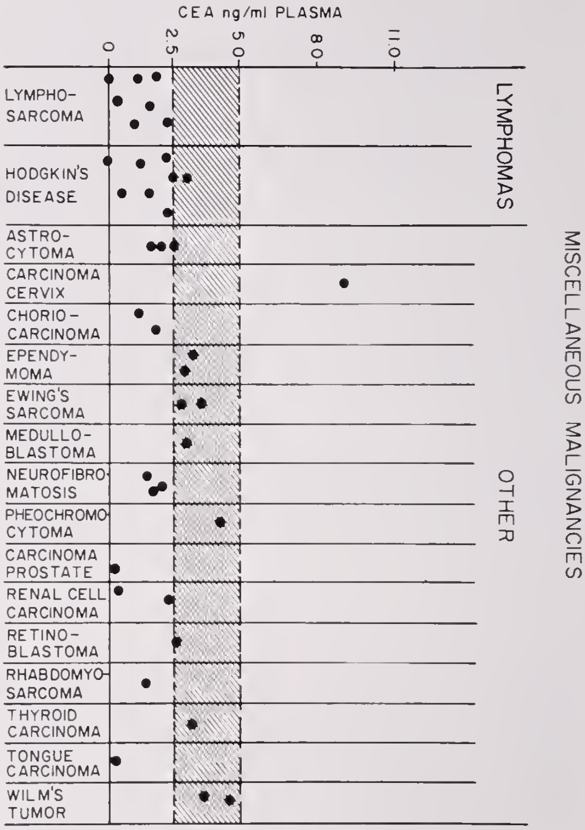

Fig. 2. Patients with most other carcinomas and noncarcinomatous malignancies (e.g. lymphomas) do not have consistently elevated levels of CEA. Again, single values in the "gray zone" may or may not represent elevated concentrations for that patient.

frozen, using dry ice in an insulated container. Plasma rather than serum samples are preferred, and the analysis of hemolyzed or heparinized specimens should be avoided.

The samples are analyzed by the zirconium phosphase gel (Z-gel) method of Hansen[5] as follows:

The CEA is extracted from the plasma specimens and allowed to react with specific CEA antiserum. ^{125}I-CEA is then added and allowed to react with the remaining CEA antiserum. The ^{125}I-CEA bound to antibody is separated from excess free ^{125}I-CEA with Z-gel, and the level of bound ^{125}I-CEA is determined by assay in a gamma scintillation spectrometer. The partition of ^{125}I-CEA between bound and free fractions is a function of the amount of CEA present in the plasma. The amount of CEA present in the plasma sample is determined from a standard inhibition curve.

Results

Fig. 1 illustrates the CEA values in a variety of malignant diseases. It is apparent from inspection of Fig. 1A that the values in patients with apparently localized disease are higher if the tumor arises in the colon or rectum, compared to values seen in patients whose primary lesion is breast, lung, or ovary. Also, patients with metastatic disease can exhibit high levels in colorectal, breast, and lung carcinoma, and in occasional neoplasms originating in the ovary, uterine cervix, and thyroid. One could generalize about these observations by saying that the test is more sensitive in patients with colorectal cancer and that the test exhibits some nonspecific positivity which is more noticeable in patients with metastatic disease.

All of the data shown in Fig. 1 represent single specimens and one can expect to encounter a considerable number of values in the "gray zone," i.e. greater than 2.5 ng/ml but less than 5.0 ng/ml. From our own experience and that of others it is likely that values in this zone represent elevated levels because when serial determinations are carried out on the same patient, the concentration often falls below 2.5 ng/ml with effective therapy.

Two important points are illustrated in Fig. 2. Serial determinations in the same patient are

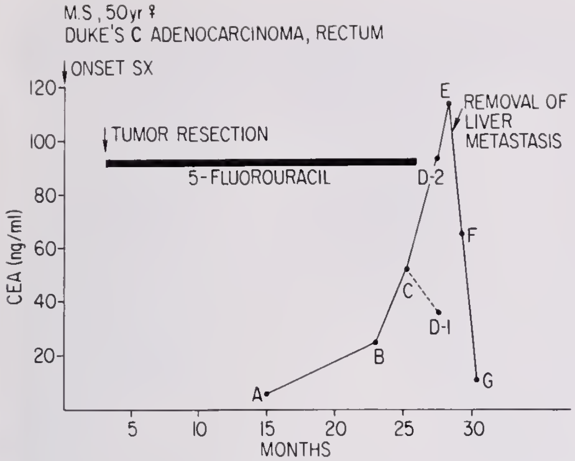

Fig. 3. Two principles of CEA assay are illustrated. (1) Serial determinations on a patient with histologically proven malignancy may be helpful in guiding therapeutic decisions; for example, in this patient other clinical parameters of metastatic disease, including liver scan, were normal at a time when the CEA was rising into a clearly abnormal range. (2) When plasma CEA concentration reaches the high range (>20.0 ng/ml) accuracy can be assured only if the assay is repeated using quantitative dilutions of the sample. The CEA value (D-1) was obtained on the undiluted sample but only when the assay is performed on a diluted sample (D-2) is the actual concentration measured with accuracy.

valuable in guiding therapy, an observation reported by others,[6] and second, it is important for the laboratory to realize that when the plasma concentration of CEA rises above 20 ng/ml the accuracy of the method may diminish because of the predictable nature of the standard inhibition curve. In other words, when the value exceeds 20 ng/ml, the laboratory should repeat the assay using dilutions of the sample in order to insure accuracy.[4]

Discussion

The development of the CEA assay has stimulated both basic research in cancer and clinical research on the effects of treatment and early diagnosis. As in the case of any diagnostic test, this assay must be considered in the light of all other clinical data—it is *not* a reliable screening test. In the patient with histologically proven malignancy, especially colorectal, pancreatic, and pulmonary carcinoma, it appears that the test has value in monitoring the efficacy of surgical, radiation, and chemical therapy.[6] Fig. 2 illustrates how serial determinations may indicate cancer recurrence and influence clinical management. The results of the Hoffmann-La-Roche, Inc. collaborative study on 10,000 patients support these conclusions,[7] and more recent data on 20,000 patients show essentially the same results.[8] ●

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Treatment of recurrent carcinoma of male breast

A Case Report

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RATIONALE FOR ORCHIECTOMY in the treatment of recurrent male breast cancer is not clear. In 1942 Farrow and Adair[1] reported rapid progression of osseous metastases when a male patient with carcinoma of the breast was treated with testosterone propionate. In a second male patient also with osseous metastases from inoperable breast carcinoma, these authors noted definite regression of the carcinoma after bilateral orchiectomy. There was marked decrease in size of the ulcerating lesion of the breast as well as calcification of the osteolytic bone lesions. There also was complete relief of pain.

This paper reports a patient treated by orchiectomy and estrogen therapy.

CASE REPORT

A 72-year-old white male was first seen in March 1967 for an ulcerating lesion of the right breast involving the nipple and underlying breast, 3.0 cm. in diameter. The lesion had been present for one year. There was no family history of breast cancer. His general health had otherwise been good. Right breast biopsy was performed followed by radical mastectomy. The pathologic diagnosis was adenocarcinoma, ductal type, with 1 of 11 axillary nodes containing carcinoma. Postoperatively, cobalt 60 was given to the right axilla and supraclavicular areas as well as to the mediastinum.

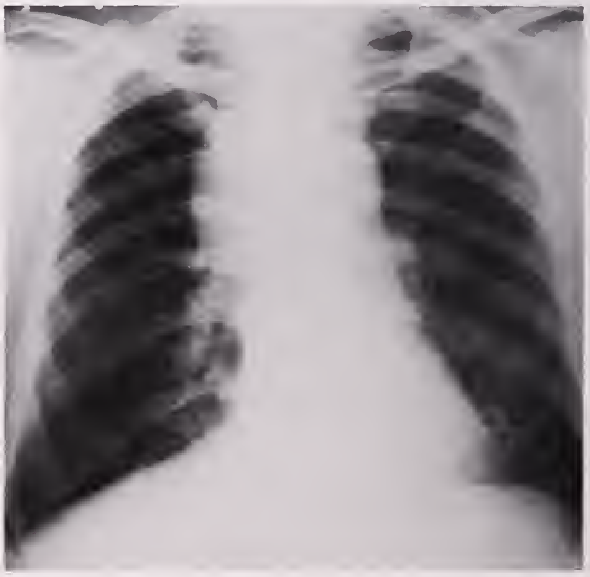

Fig. 1. May 1973, large right mediastinal mass prior to treatment with diethylstilbesterol.

Subsequently, the patient remained free of disease for four years. In March 1971, he developed numerous subcutaneous skin nodules over the posterior thorax and left supraclavicular area which proved to be metastatic nodules from his original breast cancer. Bilateral orchiectomy was performed. Within two weeks, the subcutaneous nodules were seen to be diminishing in size, and within three months, the nodules had completely disappeared.

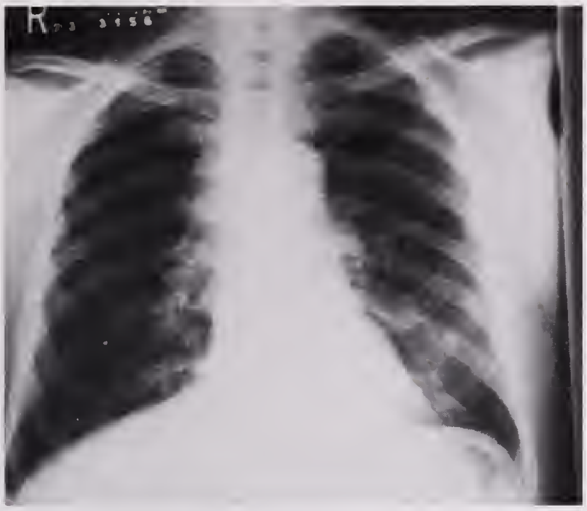

Fig. 2. June 1973, definite regression in size of mediastinal mass after three weeks of diethylstilbesterol.

The patient was free of all apparent disease for the following two years. In March 1973, the subcutaneous tumor nodules over the upper thorax recurred. He also developed a 5 cm. tumor mass in the right supraclavicular area. There was weight loss and a productive cough. X-rays of chest in May 1973 showed widespread bony metastases to the ribs and thoracic vertebrae. Also, there was a huge right anterior superior mediastinal mass measuring 6 cm. in diameter.

The patient refused chemotherapy but did agree to a trial on diethylstilbesterol. Therefore he was started on 15 mg. daily. Within three weeks, the productive cough had markedly improved, and the mass in the right supraclavicular area had almost disappeared. The subcutaneous nodules over the upper posterior thorax had also shown marked regression in size and completely disappeared after three months on this therapy. A repeat chest x-ray in June 1973 showed the large right mediastinal mass to have reduced considerably in size, and in August 1973, x-ray of the chest showed complete regression and has remained so as evident on x-ray of March 1974. The patient remains clinically free of disease, and is still being treated with diethylstilbesterol 15 mg. daily.

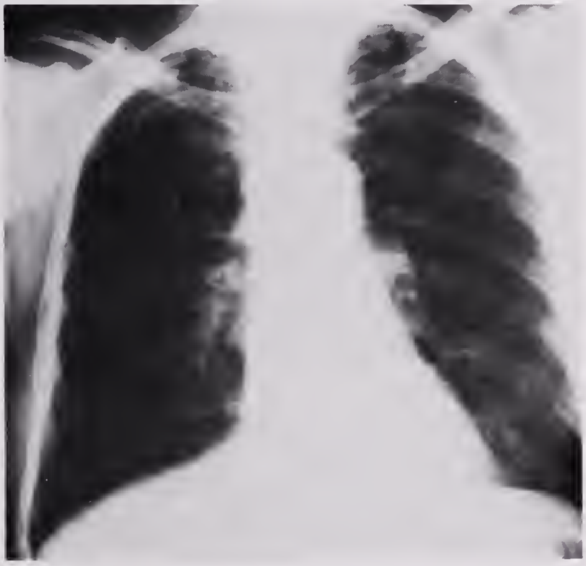

Fig. 3. August 1973, two months following diethylstilbesterol shows complete regression of the right mediastinal mass.

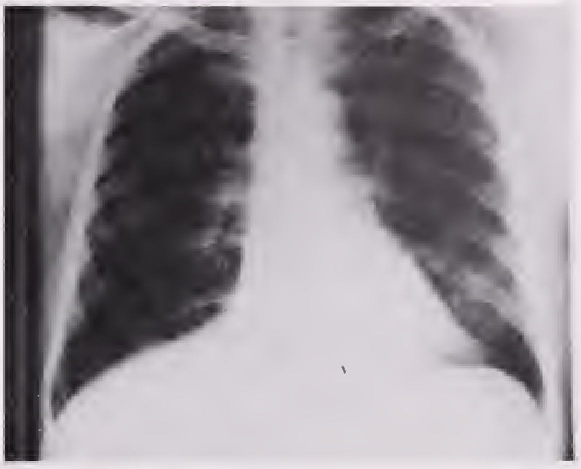

Fig. 4. March 1974, 10 months following diethylstilbesterol, a continued remission exists.

Discussion

The incidence of breast cancer in the male is about one per cent of all mammary cancer. The pathologic and clinical course of breast cancer in the male approximates that of the female.[2] The disease is rare before age 40 with a mean age of 57. This mean age is about eight years later than breast cancer in the female.[3] Of 198 males with breast cancer recorded by Memorial Hospital for Cancer and Allied Diseases, 45 per cent responded to orchiectomy. There was no response to estrogen or androgen therapy.[3]

Summary

A case of recurrent carcinoma of the male breast was treated by orchiectomy with a remission of two years. Then a second recurrence to the thoracic vertebrae, ribs, mediastinal nodes and cervical lymph nodes has resulted in a complete remission brought about by the administration of 15 mg. of diethylstilbesterol daily.

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Individual and society in biomedical progress*

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EXPERIMENTATION USING HUMAN SUBJECTS has become part and parcel of our efforts to advance medical science, psychology, and social sciences. This experimentation raises many ethical problems. The heart of these problems, I believe, lies in a deceptively simple relationship: the individual is a source of information presumably useful to society. His body, or his mind, or his social habits can yield data that can be combined with data from other subjects so as to form a statistically significant pattern that may help solve a scientific riddle or establish a therapeutic technic. Once this essential relationship between the individual as source of information and society as potential beneficiary is clearly in focus, the two most fundamental ethical questions about human experimentation become readily apparent. Does society have some claim against individual members to make the information available? Do individuals have a claim to refuse the information to society?

I shall discuss here a way of dealing with the problem of striking a moral balance between the individual's claim to personal integrity and free self-determination on the one hand and, on the other hand, society's claim to foster the common good. I shall explore this issue in relation to human experimentation, but the concepts are useful for getting a handle on several other ethical problems related to biomedical progress.

Polar Relationship of Individual Autonomy and Social Solidarity

Every society is composed of individuals. The complex relationships among individuals give shape to the society. Thus, society depends on individuals for its existence and characteristics, yet society also possesses a surprisingly independent life and power. Shaped by individuals, society shapes individuals in return by providing the necessary opportunities for actualization of the human self. The two partners of this relationship are mutually dependent and, to some extent, mutually independent. Individual autonomy and social solidarity are primary values grounded in this relationship of mutual dependence and independence.

In view of this relationship, I offer the following ethical thesis: human potential is best actualized in a moral environment structured by a *polar* relationship between individual autonomy and social solidarity.

Human potential is both the potential of individuals and the potential of mankind as a whole. Individual potential, particularly, is an intrinsic human capacity for free self-determination and for reverencing the freedom of others. Communal human potential is the power of society to promote individual well-being and to integrate individual resources for the benefit of all.

Moral environment also has a dual reference, individual and cultural. The individual moral environment is the conscience, which I understand to be a more or less coherent system of articulated moral rules together with moral sensitivities and intuitive powers. The cultural moral environment is made up of the concrete traditions, institutions, and customs by which various cultures pattern human existence in society.

A moral environment, structured by a polar tension between two values, requires that both values be maintained. It is the dual simultaneous influence of these values that is essential. The concept of polar relationship implies that the values are not reducible to one another, nor are they antagonistic to one another. Rather they stand for the essential values of two mutually dependent yet mutually distinct realities—in this instance, the individual and society. The two poles, individual autonomy and social solidarity, are values. The tension is not between the individual and society as concrete realities, but between two values which must co-exist in individual conscience on the one hand and in cultural moral patterns on the other hand.

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* Presented September 20, 1974 at the 104th Annual Session of the Colorado Medical Society. Dr. Garland, whose doctorate is in theological ethics, is Program Representative for the Bioethics Program, School of Medicine, University of California, San Francisco.

There are two implications of this proposition. On the one hand, those individual actions or those cultural patterns that collapse the polar tension in favor of individual autonomy inhibit the actualization of human potential. And, on the other hand, those individual actions and cultural patterns that collapse the polar tension in favor of social solidarity also inhibit the actualization of human potential. The point is, of course, that the collapse of the tension in favor of either pole destroys the structure of the environment. Ironically, this means that such a collapse eventually corrupts the very value in whose favor the environment shifted. Individual autonomy would be an insane autism apart from the value of social solidarity just as social solidarity would be a crushing totalitarianism apart from the value of individual autonomy.

Where does this proposition come from? What is its foundation? These questions are, I believe, too frequently left aside in many bioethics discussions. The result is an air of arbitrariness associated with appeals to principles and values, when ethical reflection moves from interpretation to critique.

As a theologian I would ultimately ground this proposition in the world view implicit in Christian faith. However, without entering into a discussion of ultimate truths, we can discern a more immediate ground in the valuation of individual freedom and social unity which at least in part inspires democratic systems such as our own and which is imbedded in our national constitution. Thus, even if we have difficulties agreeing about ultimate definitions of good and evil, we can still carry on an interpretation and critique of biomedical progress in the light of certain cultural values which we all presumably share.

Much like the therapeutic moments of examination and diagnosis, ethics consists essentially of interpretation and critique. We seek to find out what is going on in the interpretive moment. And, in the critical moment, we judge these events in relation to certain values and norms. Thus, by comparing the polar values of individual autonomy and social solidarity to the events of human experimentation, we can form judgments about whether or not we are departing from these traditional values. We can also evaluate various strategies for safeguarding these values.

Human Experimentation

In human experimentation, the subject is the source of information potentially useful to society. Does society have a claim over individuals to make themselves available as sources of information? The answer is yes and the ground for that claim is the value of social solidarity. When would social solidarity call for individuals to make themselves available as research subjects? When the information is reasonably presumed to be of benefit to society and when the autonomy of the individual would not be undetermined in the process of getting the information. Both poles must influence the judgment.

Secondly, does the individual have a claim to refuse to make presumably useful information available to society? Yes, again. And the ground for the claim is the value of individual autonomy. When would this value support refusal? Whenever individual autonomy would be threatened and when social solidarity would not be unduly neglected by refusal. Once again, both poles must play a part in forming the judgment.

Much modern concern about the ethics of human experimentation stems from the infamous Nazi medical experiments. On the level of interpretation, we would say that these experiments expressed in action the meaning that Jewish persons were non-persons, that they had no claim to individual autonomy. They could be used in any way and for any purposes the state desired. They had no right to refuse to be experimental subjects. Thus, these experiments were such that they collapsed the polarity in favor of the state or social solidarity. It is important to note that not only was the individual autonomy of these subjects ignored, but also that social solidarity was ill served as scientific investigations turned into pursuits of obsessive and sadistic curiosity.

We can discern a similar collapsed moral environment in experiments closer to home. In the now famous Tuskegee syphilis study, scientific curiosity allowed 430 individuals afflicted with syphilis to remain untreated well after an effective cure was available. This was done in order to determine scientifically the full course and consequences of untreated syphilis. The polarity collapsed in favor of a presumed social benefit. The autonomy of the individual patients seems to have counted for nothing.

The environment can collapse in the other direction as well. Individual autonomy can be given independent and unbalanced consideration. The opening sentence of the Nuremberg code is an example of collapse in this direction. Reacting to the ugly revelations about human experiments on Jewish prisoners by the Nazis, the framers of the code placed too singular an emphasis on the consent of subjects. The result was a narrow and unintentionally misleading formulation: "The voluntary consent of the subject is absolutely essential." It is misleading first because it placed a one-sided emphasis on the pole of individual autonomy. Secondly, it misleads by confusing means and ends, i.e. by identifying voluntary consent, a *means* of protecting the value of individual autonomy, with the *end*, autonomy itself.

A similar collapse of the polarity in favor of individual autonomy has produced much criticism of pediatric research in general. Since children at least up to a certain age cannot comprehend enough to consent to complicated procedures, they ought not, it is argued, be experimental subjects except where there is some direct therapeutic benefit to them. The same two problems present in the Nuremberg principle are present in this position. Individual autonomy is considered in isolation from social solidarity, and consent is confused with autonomy.

The confusion of consent (the means) with individual autonomy (the end) creates problems in many other areas of medical research such as trauma work and some psychiatric work and other areas where the subject is either unconscious or in a situation where emotion is likely to cloud judgment and render consent questionable. Consent is a means of promoting the value of individual autonomy. Consent is not an end in itself. It is not even an indispensable means to this end. There are other effective means to protect the individual's autonomy and his claim to refuse to be an experimental subject. Prior review of research projects is a means of protecting the individual autonomy of potential subjects, as are parental or guardian approval, a special subjects' advocate, and, indispensably, the personal and professional ethics of the investigator. All of these can work in various combinations to generate adequate protection of the autonomy of individual subjects.

The concept of a polar frame of reference or moral environment does not solve all the problems associated with the ethics of human experimentation. But it does help organize the problems, facilitate reflection, and focus discussion of very complicated matters.

I believe this concept is particularly useful on two scores. First, it draws our attention to the values at stake. Secondly, it constrains us to hold together these distinguishable but inseparable values. These two functions can help avoid two basic pitfalls in discussions of the ethics of human experimentation. The first pitfall is that of absolutizing either individual autonomy or social solidarity. One frequently sees this being done in theory and debate, resulting in confusing and unbalanced policies, codes, and guidelines. The second pitfall is that of confusing means and ends. The values are the ends to be sought, promoted, or protected. There are often a number of means or strategies that can achieve this purpose. It is surprisingly easy to let a strategy become an end in itself and to invest it with undue importance.

I believe that the clarity this concept seeks to develop is important for the ongoing debates, discussions, and decisions by which we attempt to correlate our beliefs and values with our actions in the pursuit of biomedical progress. We all hold bits of information that need to be worked together into consistent meanings. Clarity about the values we are attempting to pursue will help all of us interpret and critique both goals and strategies. We all need each other's perspectives and insights. We need to hear and address one another as fellow valuers both of the autonomy of each individual and of the social solidarity by which we all benefit.

Conclusion

Besides human experimentation, many other aspects of biomedical progress and policy are involved in the polarity of individual autonomy and social solidarity. In the area of genetics many of the amazing possibilities of intervention and control raise the question whether we should do everything that we can do. We face a population crisis that threatens to be resolved by disaster if human decisions do not take control of growth factors. Yet how should we go about limiting the freedom of individual couples to procreate?

New psychological and surgical technics for behavior control lead to questions about how far to go in controlling others. Who will control the controllers? Similarly, computer data collection, comparison, and retrieval offer promise for more efficient health care delivery. But how shall we set boundaries between our private and public selves lest we find ourselves living out an Orwellian scenario with Big Brother aware of every move we make? In this age of transplants, how exclusive a right does an individual have over his organs? Dare we refuse to some persons the freedom to go to their graves with all their bodily parts?

Biomedical progress in our day continuously raises ethical questions related to the polarity of individual autonomy and social solidarity. We may fail on either side of the polarity. In doing so, we will find ethical meanings being expressed that negate our valuations of individual freedom and social unity. As such they represent, I believe, a cost too dear to justify their contribution, no matter how dramatic, to the work of biomedical progress.

Summary

Biomedical progress involves us in the problem of determining the moral relationship between the individual and society. Discussions of these issues, especially in the matter of human experimentation, tend to deal separately with the values of individual autonomy and social solidarity. Human potential is best served when these values are held in polar relation both within individual conscience and in social institutions.

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MATERNAL MORTALITY

The following case has been reviewed by the Colorado Maternal Mortality Committee* and selected for publication because of its educational value.

A 21-YEAR-OLD GRAVIDA THREE, para one, aborta one, visited her local medical doctor in February, 1974. Diagnosis of early pregnancy and mild anemia was made. She was given prenatal vitamins. One week later she was treated with antibiotics for a swollen, tender anterior cervical node, although no focus of infection could be found. A good response to the antibiotics was noted. Two weeks later she developed a bruise on her thigh followed in one week by several more bruises. She was thereupon referred to an internist who found a low hematocrit. Bone marrow biopsy disclosed acute granulocytic leukemia. She was referred to a medical center for definitive treatment on March 1, 1974.

During her hospitalization she received a current chemotherapeutic treatment regimen of Ara C (Cystosine Arabinoside), Thioguanine, Allopurinol, and Prednisone. Hematocrit of 18 upon admission was improved by transfusions to 33. By date she was 19 weeks pregnant, 14 to 15 weeks by examination, and 16 weeks by ultrasound. Abortion was considered at this time, but was determined to be too risky. The plan was to recommend abortion later should she agree and should she have a remission.

At her second admission on March 29th she received blood transfusions until hematocrit of 19 was improved to 33. Ultrasound measured 18 weeks, and abortion was considered hazardous at this admission, although the hematologist recommended abortion with remission. Both parents refused abortion, however. After much discussion, chemotherapy was not considered to be damaging the fetus at this time. The patient developed a bilateral maxillary sinusitis which was treated with Cleocin and Valium.

The third admission in April was because of enlarged anterior cervical nodes. She was treated with Percodan and aspirin. Ultrasound measured 18-20 weeks.

The last admission was manifested by nausea and vomiting. A third course of therapy was begun on the third of May. The patient noted a lack of fetal movement, soon thereupon went into shock which defied the usual treatments, including gentamicin Cleocin, steroids, platelets, wholeblood, colloids with monitoring by central venous catheter. Paracentesis disclosed a serous abdominal fluid without bacteria, and exploratory celiotomy showed a hemorrhagic small bowel and normal uterus.

The patient expired four hours postoperatively. Autopsy reported loss of blood supply to the small bowel, acute granulocytic leukemia, normal uterus and fetus.

The Committee believes that the management of this patient was complete and thorough. Opinion that an earlier abortion might have influenced the course of the leukemia and thus have brought about a remission was discussed. Of course, both the patient and her husband at a later time refused this method of treatment.

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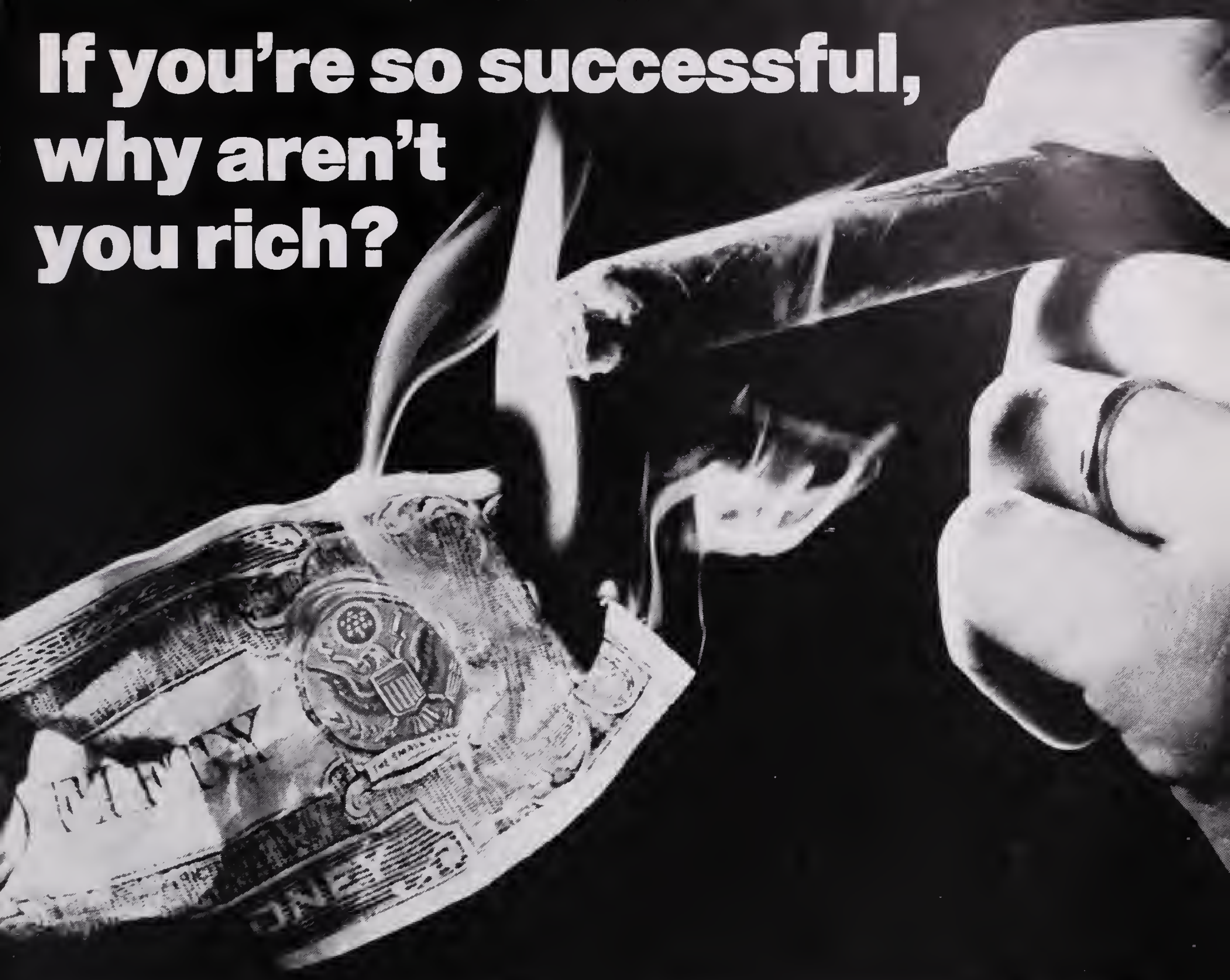
*The following physicians have been appointed to serve on the Maternal Mortality Committee, a subcommittee under Maternal and Child Health: Lawrence W. Roessing, Jr., Chairman, Maxwell A. Abelman, L. Joseph Butterfield, Gerard W. del Junco, Watson A. Bowes, Jr., Horace E. Thompson, all of Denver; John H. Darst, Greeley; Walter J. Grund, Littleton; Mallory T. Harling, Fort Collins; Ronald E. Harrington, Boulder; James R. Patterson, Englewood; Edwin N. Running, Jr., Arvada; Louis C. Wollenweber, Jr., Lakewood; Thomas F. Purdon, Colorado Springs.



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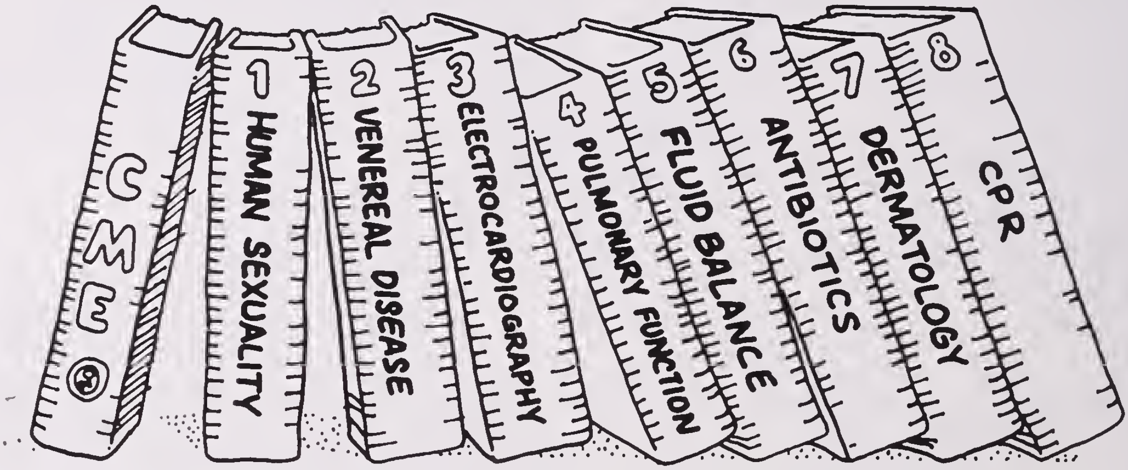

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8. Basic and Advanced Life Support — Cardiopulmonary Resuscitation (CPR)

*Courses 1 through 7 are 6 hours each; each is presented twice (once on Saturday, once on Sunday). Course No. 8 is a 12-hour course that runs both days.

Sites

Tampa, Fla. - February 8-9, 1975
Phoenix, Ariz. - March 15-16, 1975
Minneapolis, Minn. - July 26-27, 1975
Williamsburg, Va. - September 27-28, 1975

For more information **WRITE:**

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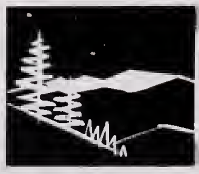

COLORADO

Full Time Doctor For Pilots

The noted aerospace medicine specialist, Dr. Richard L. Masters, has established full time headquarters in Denver, Colorado, where he will devote full time to aero medical programs for the Air Line Pilots Association.

Dr. Masters has gained national recognition as an authority in aerospace medicine, for airline pilots in particular, since joining the Lovelace Clinic, Albuquerque, New Mexico, six years ago. He became medical advisor to ALPA in August 1969 and has spearheaded research in preventive health programs for airline pilots. He has undertaken special projects dealing with preventive cardiology and human factors in aviation accidents on behalf of ALPA.

In his independent status, he will expand these current programs to embrace broader aspects of pilot health care not possible before, because of his former duties as chairman of the Department of Aerospace and Preventive Medicine at Lovelace Clinic.

Joseph A. Pickersgill has joined him as Administrative Assistant.

Masters received his doctorate in medicine from the University of Michigan and his Masters of Public Health degree from Harvard University. He is a fellow of the American College of Preventive Medicine and of the Aerospace Medical Association. The Denver offices will be located at: Suite 117, 12000 East 47th Avenue.

MEDICAL SCHOOL NOTES

Maaske and Kotin Named

Dr. Clarence Maaske was named professor of physiology emeritus and Dr. Paul Kotin was named professor adjoint of pathology during the October 29 meeting of the University of Colorado Regents at the CU Medical Center.

Retired director of the Student Advisory Office, Dr. Maaske was appointed to the CU medical faculty in 1945 as associate professor of physiology and pharmacology. He was named chairman of the Department of Physiology when it was created in 1952. From 1972 to 1974, he was director of the Student Advisory Office. A fellow of the American Association for the Advancement of Science, Dr. Maaske's other affiliations include the American Physiological Society, Society for Experimental Biology and Medicine, American Heart Association, Sigma Xi scientific honorary, Alpha Omega Alpha medical honorary, and Phi Sigma and Gamma Alpha, professional societies in biology.

A physician for the Johns-Manville Corporation, Dr. Kotin served from 1971 to 1973 as dean of the School of Medicine and from 1971 to 1974 as vice president for health sciences at Temple University, Philadelphia, Pa. He is a former associate director for field studies and former scientific director for etiology at the National Cancer Institute, Bethesda, Md. A member of Alpha Omega Alpha and Sigma Xi, Dr. Kotin also belongs to the American Association for the Advancement of Science, American Association for Cancer Research, American Society for Experimental Pathology, and other professional organizations.

Clinical Faculty Awards

A pediatrician and an orthopedic surgeon received the outstanding clinical faculty awards in November during the annual medical staff meeting of the University of Colorado Hospitals held at the University Club.

Recipients were Dr. James E. Strain, chairman of the committee on clinical faculty affairs, CU Department of Pediatrics, and Dr. Foster Matchett, CU clinical associate professor of orthopedics emeritus.

A member of the Colorado Commission on Children and Youth, Dr. Strain received his MD degree from CU. He is the chairman of the long range planning committee of the American Academy of Pediatrics, and chairman of the American Medical Association's Section Council on Pediatrics. Dr. Strain belongs to several organizations, including the American Academy of Pediatrics, AMA, Denver County Medical Society, and the Colorado State Medical Society. A clinical professor of pediatrics, Dr. Strain is a past president of the medical board at Colorado General Hospital, and a past president of the Rocky Mountain Pediatric Society. He also is a Head Start consultant for the American Academy of Pediatrics.

Dr. Matchett, who received his MD degree from the University of Nebraska, served for 30 years on the orthopedic service in the CU School of Medicine prior to his appointment in 1968 as clinical associate professor of orthopedics emeritus. He is a former chief of orthopedic surgery at Denver General Hospital, and currently is a consultant to the VA Hospital and Fitzsimons Army Medical Center. A member of the American Academy of Orthopedic Surgeons, Dr. Matchett also belongs to the AMA, Western Orthopedic Society, Colorado State Medical Society, and Denver County Medical Society. He is a past president of the Rocky Mountain Orthopedic Society, and an AMA diplomate in orthopedic surgery.

Both award recipients are members of Alpha Omega Alpha, honorary medical society.

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THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Analysis of Roentgen Signs: Meschan, Isadore. Philadelphia, Saunders, 1974. 3 v. $70.00.

Anesthesia For Outpatient Surgery: Cohen, David D. Springfield, Ill., Thomas, 1970. 67 p. $3.50.

Atlas of External Diseases of the Eye: Donaldson, David D. St. Louis, Mosby, 1966. vol. 1 **Congenital Anomalies and Systemic Diseases.**

Atlas of Hand Surgery: Chase, Robert A. Philadelphia, Saunders, 1973. 438 p. $30.00.

Best & Taylor's Physiological Basis of Medical Practice, 9th ed.: Brobeck, John, ed. Baltimore, Williams and Wilkins, 1973. various pagings. $22.00.

Chest Roentgenology: Felson, Benjamin. Philadelphia, Saunders, 1973. 574 p. $17.00.

Controversy in Obstetrics and Gynecology II: Reid, Duncan E., ed. Philadelphia, Saunders, 1974. 854 p. $28.00.

Corneal and External Diseases of the Eye: Polack, Frank M., ed. Springfield, Ill., Thomas, 1970. 383 p. $11.50.

Diseases of the Breast: 2nd ed.—revised reprint. Haagensen, C. D. Philadelphia, Saunders, 1974. 829 p. $37.50.

Diseases of Metabolism, 7th ed.: Duncan, Garfield G. Edited by Philip K. Bondy in association with Leon E. Rosenberg. Philadelphia, Saunders, 1974. 2 v. $52.00.

General Ophthalmology, 7th ed.: Vaughan, Daniel, ed. Los Altos, Calif., Lange, 1974. 334 p. $9.50.

Handbook of Medical Treatment, 14th ed.: Chatton, Milton, Los Altos, Calif., Lange, 1974. 640 p. $6.50.

Handbook of Obstetrics and Gynecology, 5th ed.: Benson, Ralph C. Los Altos, Calif., Lange, 1974. 770 p. $8.00.

Handbook of Psychiatry, 3rd ed.: Solomon, Philip, ed. Los Altos, Calif., Lange, 1974. 705 p. $8.00.

Harrison's Principles of Internal Medicine, 7th ed.: Wintrobe, Maxwell M., ed. New York, McGraw-Hill, 1974. 2 v. $35.00.

Interpretation of Schizophrenia, 2nd ed., completely revised and expanded. Arieti, Silvana. New York, Basic Books, 1974. 756 p.

Lupus Erythematosus; A Review of the Current Status of Discoid and Systemic Lupus Erythematoses and Their Variants, 2nd ed.: Dubois, Edmund L., ed. Los Angeles, Univ. of Southern Calif. Press, 1974. 798 p. $36.00.

Lymphatics in Cancer: By C. D. Haagensen and others. Philadelphia, Saunders, 1972. 583 p. $30.00.

Management of Thoracic Injuries: Hood, R. Maurice, ed. Springfield, Thomas, 1969. 188 p. $9.25.

Ophthalmic Manifestations of Systemic Vascular Disease: Cogan, David G. Philadelphia, Saunders, 1974. (**Major Problems in Internal Medicine,** vol. 3).

Organizational Issues in the Delivery of Health Services: Zola, Irving K., ed. New York, Milbank, 1974. 393 p. Gift.

Pathologic Basis of Disease: Robbins, Stanley, Philadelphia, Saunders, 1974. 1595 p. $27.50.

Pathologic Physiology, Mechanisms of Disease, 5th ed.: Sodeman, William S., Philadelphia, Saunders, 1974. 1013 p. $25.00.

Pediatric Cardiology, 3rd ed.: Nadas, Alexander. Philadelphia, Saunders, 1972. 749 p. $25.00.

Psychology of Ethics: Dorsey, John M. Detroit, Center for Health Education, 1974. 261 p. Gift of Dr. Billings.

Questions and Answers on Death and Dying: Kubler-Ross, Elisabeth. New York, MacMillan, 1974. 177 p. $1.50.

Surgery of the Hip Joint: Tronzo, Raymond G. Philadelphia, Lea and Febiger, 1973. 840 p. $49.50.

The library has received an NLM Literature Search entitled "PSRO's".

Book Review

Chest Roentgenology, by Benjamin Felson, MD. 574 p. W. B. Saunders Company, Philadelphia, 1973. $17.00.

In his own inimitable way, Dr. Felson has given us another valuable teaching instrument. This book, originally planned as the second edition of his *Fundamentals of Chest Roentgenology,* has resulted in one of the most complete texts referable to chest pathology, radiology and x-ray interpretation that is available today.

The topics are arranged in an unusual, but surprisingly practical, order by perspective and anatomic units. It is highly readable, easily understood, challenging by its veritable multiplicity of important details. The descriptive text is accompanied by literally hundreds of illustrations, all clear and clearly correlated with the text. Additionally, Dr. Felson's ever-present wit is sprinkled throughout, always at just the properly spaced interval to awaken the reader from the intense concentration needed to absorb each detail. It is an enjoyable book to read and is extremely worthwhile as a classic reference for anyone concerned with chest x-ray interpretation-students, house staff of most specialties, radiologists, and physicians in almost any endeavor of practice. There is much to be learned about chest pathology and normal anatomy subtly interwoven under the guise of appearance of the chest roentgenogram.

W. Gerald Rainer, MD

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Opinion & Dialogue

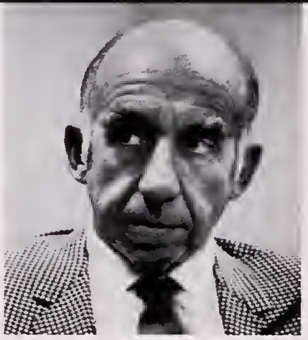
The Role of the Detail Man

Dr. Willard Gobbell
Family Physician
Encino, California

"I may be prejudiced, but I ar very much in favor of the detail me I meet. Most of them are knowledg able about the drugs they promote and can be a great help in acquainting me with new medication."

Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the years I have gotten to know most of the men who visit me regularly and they in turn have become aware of my particular interests and the nature of my practice. They, therefore, limit their discussion as much as possible to the areas of interest to me. Since I usually see the same representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Jeremiah Stamler
Chairman
Department of Community Health and Preventive Medicine, and Dingman Professor of Cardiology
Northwestern University Medical School

"In the total picture of dealing with health problems in this countr, there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharmaceutical industry is the type of contact that people in a medical center, research people, and academic people have and that's in all likeliho on a somewhat different level from that of the practicing physician.

Let me touch on how I personally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real educational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent films produced by the pharmaceutical industry. When they function in this

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

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capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.,* the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

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Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

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Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride ...... 2.5 mg.
(Warning: May be habit forming)
atropine sulfate .... 0.025 mg.

Usually stops diarrhea promptly.

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL *IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. *Liquid,* 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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MEETINGS

American College of Emergency Physicians-Emergency Department Nurses' Association

FIRST ANNUAL ROCKY MOUNTAIN CONFERENCE ON EMERGENCY MEDICINE

Manor Vail, Vail, Colorado

January 19-22, 1975

Contact: Ellen H. Taliaferro, MD, Ambulatory Care Services, St. Joseph Hospital, 18th and Franklin Streets, Denver, Colorado 80218.

Colorado Association for Continuing Medical Laboratory Education

SELECTED TOPICS IN HEMATOLOGY

Hilton Inn, Vail, Colorado

January 20-22, 1975

Contact: CACMLE, Inc., Box 84, Mercy School of Nursing Building, 1601 Milwaukee St., Denver, Colorado 80206.

Intermountain Thoracic Society

THE 18TH ANNUAL MID-WINTER CONFERENCE ON CHEST DISEASE

Snowbird Ski Resort, Utah

January 22-25, 1975

Contact: Franklin K. Brough, Intermountain Thoracic Society, 1616 S. 11th East, Salt Lake City, Utah 84105.

Colorado Heart Association

HIGH-COUNTRY CARDIAC CONFERENCE

Manor Vail and Hilton Inn, Vail, Colorado

January 23-25, 1975

Contact: Colorado Heart Association, 4521 East Virginia Avenue, Denver, Colorado 80222.

Rocky Mountain Academy of Industrial Medicine—Colorado Medical Society

10TH ANNUAL INSTITUTE OF INDUSTRIAL MEDICINE

The Broadmoor, Colorado Springs, Colorado

January 23-24, 1975

Contact: R. J. Zarlengo, MD, Rocky Mountain Academy of Industrial Medicine, 111 Havana St., Aurora, Colorado 80010.

Credit: 7½ hours elective AAFP; 6 hours Physician's Recognition Award—AMA

Colorado Ophthalmological Society

MIDWINTER SEMINAR IN OPHTHALMOLOGY

Snowmass-at-Aspen, Colorado

January 26-30, 1975

Contact: Colorado Ophthalmological Society, 1601 East 19th Avenue, Denver, Colorado 80218.

General Rose Memorial Hospital Department of Surgery

NASAL SYMPOSIUM

Stouffer's Denver Inn, 3203 Quebec,

Denver, Colorado

February 6-7, 1975

The Lodge at Vail, Vail, Colorado,

February 8-12, 1975

Contact: Division of Continuing Medical Education, General Rose Memorial Hospital, 1050 Clermont St., Denver, Colorado 80220.

University of New Mexico

ROCKY MOUNTAIN NEURO-OPHTHALMOLOGY COURSE

Hilton Inn, Santa Fe, New Mexico

February 6-8, 1975

Contact: Neuro-Ophthalmology Course, Department of Neurology, 1007 Stanford Dr., N.E., Albuquerque, New Mexico 87131.

American Academy of Orthopaedic Surgeons

SKIING INJURIES

Snowmass-at-Aspen, Colorado

February 10-13, 1975

Contact: American Academy of Orthopaedic Surgeons, 430 North Michigan Avenue, Chicago, Illinois 60611.

Albuquerque and Bernalillo County Medical Association

TAOS MEDICAL-SKI SYMPOSIUM

Taos, New Mexico

February 12-15, 1975

Contact: Thomas A. Bodnar, Albuquerque and Bernalillo County Medical Association, 3010 Monte Vista Blvd., N.E., Albuquerque, New Mexico 87106.

University of Utah College of Medicine, Department of Anesthesiology

20TH ANNUAL ANESTHESIOLOGY COURSE

C'est Bon Hotel Convention Center,

Park City, Utah

February 14-18, 1975

Contact: Department of Anesthesiology, University of Utah Medical Center, 50 North Medical Drive, Salt Lake City, Utah 84132.

Colorado Medical Society

WINTER CLINICS

Swedish Medical Center Complex
501 East Hampden Avenue, Englewood, Colorado

February 28-March 2, 1975

Contact: Mrs. Shirlee Myers, Colorado Medical Society, 1601 East 19th Avenue, Denver, Colorado 80218.

Beth Israel Hospital Foundation

ASPEN RADIOLOGY CONFERENCE

Aspen Institute for Humanistic Studies, Aspen, Colorado

March 3-7, 1975

Contact: Maurice O'Connor, MD, Conference Director, Division of Radiology, Denver General Hospital, Denver, Colorado 80204.

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OBITUARIES

E. Bruce Badger, MD, well known in internal medical circles around Denver, died Friday, November 15, 1974 in the Labette County Medical Center in Parsons, Kansas. He had practiced internal medicine in Denver until about twelve months ago when ill health forced him to seek a different type of life. He became director of the Southeast Kansas Tuberculosis Hospital in Chanute, Kansas, a position he held until his death.

Born in Carbondale, Colorado, March 11, 1905, and educated in the public schools of that community, he entered the University of Kansas at Lawrence after graduating from high school in 1923. After receiving his BA degree, he taught school in the Carbondale area for three years before entering the University of Kansas School of Medicine from which he received his MD in 1932.

He served in the U.S. Army until after World War II, achieving the rank of Lieutenant Colonel. Following the war he took a couple of years of graduate training at the University of Colorado Medical Center, qualifying as an internist.

Dr. Badger was a member of the Denver County and Colorado medical societies, and of the American Medical Association. Also he belonged to the Colorado Society of Internal Medicine, and the American Society of Internal Medicine. For years he was an active staff member at St. Luke's Hospital in Denver, and was a member of the honorary staff at the time of his death.

He was a Mason belonging to the Lodge in Carbondale and to the Shrine. He belonged to Christ Methodist Church, Denver.

In June 1932 he was married to Mildred Beverly Jones in Kansas City, Kansas. Mrs. Badger survives as do a son John Bruce of Denver, and two sisters, Mrs. Charles Perry, Waverly, Kansas, and Mrs. William Perry, Carbondale.

* * *

J. Rowan Haney, MD, of Colorado Springs died at his home Friday, November 15, 1974 after a long illness. He was 89 years of age. He was born in Alabama, July 9, 1885, and was educated in the public schools of Alabama and Mississippi. He attended Jefferson Medical College in Philadelphia, Pennsylvania from which he was graduated in 1910.

Dr. Haney's family had been impoverished in the Civil War, and there were no funds to pay for the education he desired. Being an advocate of physical fitness, he had constructed a trapeze and horizontal bars in the family backyard where he spent hours mastering sundry gymnastic procedures. When the time came for him to enter the University, he succeeded in being appointed Director of Gymnastics at a monthly salary of $125.00. This enabled him to complete his college and medical school training.

After graduation in 1910 he established a practice in Clovis, New Mexico. In 1917 he moved to Colorado City, an area now part of Colorado Springs. A year later the great "Flu Epidemic" hit the United States as it did the rest of the world, leaving many respiratory cripples. These, added to the host of "lungers" who had been coming to Colorado for years to "chase the cure," constituted a clientele in need of special attention. Since there were no specialists in those days, most all doctors treated whatever came along. Dr. Haney was among the pioneers in the use of pneumothorax for management of tuberculosis.

He was the last surviving founding member of the El Paso County Medical Society. He was also an original member of the staffs of both Penrose and Memorial Hospitals where he on occasions held the position of Chief of Staff.

Dr. Haney's widow, Mrs. Katherine Haney, survives him as do two daughters, Mrs. Katherine Magruder of Colorado Springs and Mrs. David Roberts of Boulder; a son Lawrence Haney, MD, of Colorado Springs. Eight grandchildren and six great grandchildren also survive the doctor.

* * *

Jesse Waydelich White, MD, died October 18, 1974 in Pueblo of a heart attack at the age of 74. Born February 2, 1900 in Livingston County, Missouri, educated in the public schools of that district, he acquired a BA degree from the University of Missouri at Columbia in 1922. He then attended Yale University in New Haven, Conn. where he was awarded his MD in 1924. Following an internship and a surgical residency at St. Luke's Hospital, St. Louis, Mo., he started practicing in Pueblo in 1926. As time went on he limited his practice to general surgery and obstetrics and gynecology.

Dr. White was a member of the Pueblo County and Colorado medical societies, and of the American Medical Association. He was also a Fellow of the American College of Surgeons and a member of the Southwest Surgical Congress. He belonged to the Alpha Kappa Kappa professional medical fraternity and to Sigma Xi. He belonged to the Methodist Church, the Kiwanis Club, the Knife and Fork Club, and the Pueblo Rockhounds Club. He served the Pueblo County Medical Society, both as secretary and president.

He was married to Olivene Slater of Pueblo on September 8, 1945. Mrs. White survives as do a son Richard, Pueblo, and daughter, Mrs. Nancy Stone of Omaha, Nebraska, and four grandchildren.

SOCIETY OFFICERS

Colorado Medical Society

OFFICERS—1974-75—terms of Officers and Committeemen expire at the Annual Session of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: Howard T. Robertson, Denver.

President-elect: Joseph S. Pollard, Jr., Colorado Springs.

Vice President: Harlan B. Huskey, Fruita.

Treasurer: Otis J. King, Jr., Colorado Springs.

Constitutional Secretary: Stanley J. Sontag, Lakewood.

Delegates to the A.M.A.: John M. Wood, Englewood, Dec. 31. 1975; Robert E. McCurdy, Denver, Dec. 31, 1975; Kenneth A. Platt, Westminster, Jan. 1, 1975-Dec. 31, 1976.

Alternate Delegates to the A.M.A.: Kenneth A. Platt, Westminster, Dec. 31, 1974; Clyde E. Stanfield, Denver, Dec. 31, 1976; William Y. Takahashi, Boulder, Dec. 31, 1975; Joseph L. Kovarik, Dec. 31, 1975. One position to be filled.

Speaker, House of Delegates: Robert A. O'Dell, Aurora.

Vice Speaker, House of Delegates: R. Jack Warren, Denver.

Foundation Advocate: H. Sol Cersonsky, Denver.

Scientific Editor for Colorado and Chairman of the Editorial Board, Rocky Mountain Medical Journal: Carl H. McLauthlin, Denver.

Scientific Editor Emeritus, Rocky Mountain Medical Journal: Douglas Macomber, Denver.

Executive Director: Mr. Donald G. Derry, 1601 East 19th Avenue, Denver, Colorado 80218. Telephone (303) 534-8580.

New Mexico Medical Society

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Session in the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: U. G. Hodgin, Jr., Albuquerque.

President-elect: Robert Cutler, Espanola.

Vice President: Walter Hopkins, Lovington.

Secretary-Treasurer: Ronald V. Dorn, Jr., Albuquerque.

Immediate Past President: Armin T. Keil, Raton.

Speaker, House of Delegates: William J. Hossley, Deming.

Vice Speaker, House of Delegates: John D. Abrums, Albuquerque.

Delegate to A.M.A.: Emmit M. Jennings, Roswell.

Alternate Delegate to A.M.A.: Armin T. Keil, Raton.

Councilors for Three Years: George P. Bunch, Las Vegas; Robert Zone, Santa Fe; Livingston Parsons, Albuquerque; John Moore, Roswell.

Councilors for Two Years: James Loucks, Los Alamos; William C. Gorman, Albuquerque; Donald Wolfel, Albuquerque; James Gaba, Artesia; Jerome P. Pucelik, Las Cruces; Theodore Draelos, Silver City; Donald Draney, Alamogordo.

Councilors for One Year: Edgar Smith, Albuquerque; John G. Griffin, Albuquerque; Samuel Neff, Clovis; T. G. McCormick, Hobbs; Norton Ritter, Gallup; Jack Coats, Farmington.

Scientific Editor for New Mexico Rocky Mountain Medical Journal: Marcus J. Smith, Santa Fe.

Assistant Scientific Editor for New Mexico, Rocky Mountain Medical Journal: William S. Curran, Albuquerque.

Associate Editor for New Mexico, Rocky Mountain Medical Journal: Mr. Ralph R. Marshall, Albuquerque.

Executive Director: Mr. Ralph R. Marshall, 3010 Monte Vista Blvd., NE, Albuquerque, 87106. Telephone (505) 265-8494.

Associate Executive Director: Rick Beitler, Albuquerque.

Montana Medical Association

OFFICERS—1974-75—Terms of Officers and Committemen expire at the Annual Meeting of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Meeting.

President: John R. Halseth, Great Falls.

President-elect: David Gregory, Glasgow.

Vice President: Colvin H. Agnew, Billings.

Secretary-Treasurer: Robert P. Yost, Missoula.

Assistant-Secretary-Treasurer: James E. Elliott, Havre.

Delegate to the A.M.A.: Herbert T. Caraway, Billings.

Alternate Delegate to the A.M.A.: Mark B. Listerud, Wolf Point.

Executive Committee: John R. Halseth, Great Falls; David Gregory, Glasgow; Colvin H. Agnew, Billings; Robert P. Yost, Missoula; James E. Elliott, Havre; Herbert T. Caraway, Billings; Mark B. Listerud, Wolf Point; John R. Burgess, Jr., Helena; James K. Cope, Forsyth.

Scientific Editor for Montana, Rocky Mountain Medical Journal: Gerald A. Diettert, Missoula.

Associate Editor, Rocky Mountain Medical Journal: Mr. G. Brian Zins, Helena.

Executive Director: Mr. G. Brian Zins, 2021 11th Avenue, Suite 12, Helena, Montana 59601, Teelphone (406) 443-4000.

Nevada State Medical Association

OFFICERS—Terms of Officers and Committeemen expire in April 1976.

President: William K. Stephan, Las Vegas.

President-elect: John W. Callister, Reno.

Secretary-Treasurer: John L. Holmes, Las Vegas.

Immediate Past President: Thomas K. Hood, Elko.

Delegate to A.M.A.: Norman Christensen, East Ely.

Alternate Delegate to A.M.A.: Richard C. Inskip, Reno.

Scientific Editor for Nevada, Rocky Mountain Medical Journal: Thomas J. Scully, Reno.

Assistant Scientific Editor for Nevada, Rocky Mountain Medical Journal: Robert W. Williams, Las Vegas.

Associate Editor, Rocky Mountain Medical Journal: Mr. Richard G. Pugh, Reno.

Executive Director: Mr. Richard G. Pugh, 3660 Baker Lane, Reno 89502. Telephone (702) 825-6788.

Wyoming State Medical Society

OFFICERS—1975—Terms of Officers and Committeemen expire December 31, 1975. Terms of office (with the exception of Delegate and Alternate Delegate to A.M.A.) expire at the end of the calendar year rather than at the Annual Session.

President: Donald B. Hunton, Cheyenne.

President-elect: Patrick D. Nolan, Buffalo.

Vice President: James E. Stoetzel, Pine Bluffs.

Secretary: Kent T. Christensen, Casper.

Treasurer: James R. Alexander, Torrington.

Delegate to A.M.A.: Fenworth M. Downing, Sheridan.

Alternate Delegate to A.M.A.: John J. Corbett, Casper.

Speaker of the House: Theodore L. Johnston, Cheyenne.

Vice Speaker of the House: Ross J. Collie, Lander.

Immediate Past President: Paul R. Yedinak, Rock Springs.

Scientific Editor for Wyoming, Rocky Mountain Medical Journal: Francis A. Barrett, Cheyenne.

Associate Editor for Wyoming, Rocky Mountain Medical Journal: Mr. Robert Smith, Cheyenne.

Executive Director: Mr. Robert Smith, P. O. Drawer 4009, Cheyenne, Wyoming 82001. Telephone (307) 635-2424.

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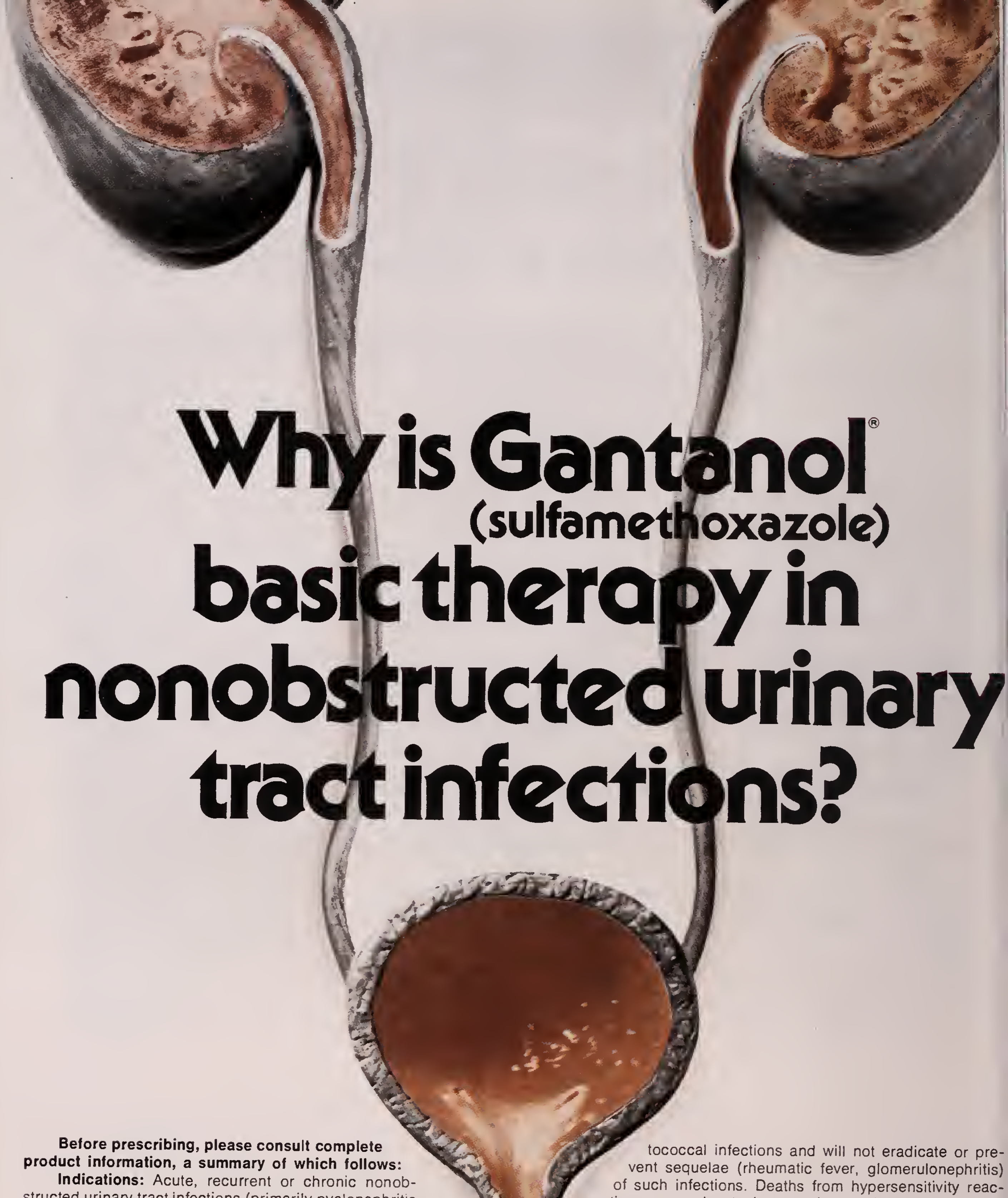

Why is Gantanol® (sulfamethoxazole) basic therapy in nonobstructed urinary tract infections?

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. **Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, pur-

Because it is considered a good choice...

- for efficacy in nonobstructed cystitis, pyelonephritis and pyelitis
- for control of susceptible *E. coli, Klebsiella-Aerobacter, Staph. aureus, Proteus mirabilis* and, less frequently, *Proteus vulgaris*
- for prompt antibacterial blood and urine levels in from 2 to 3 hours after initial 2-gram adult dose
- for economical around-the-clock coverage
- for maximum patient cooperation with easy-to-remember B.I.D. dosage

Basic Therapy

Gantanol®

(sulfamethoxazole)

Tablets/Suspension
(0.5 Gm) (0.5 Gm/teasp.)

pura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Nutley, N.J. 07110

KEEP THE HYPERTENSIVE PATIENT ON THERAPY KEEP THERAPY SIMPLE WITH

DYAZIDE®

Trademark

Each capsule contains 50 mg. of Dyrenium® (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Just 'Dyazide' once daily or twice daily
No inconvenient potassium supplements
Nor special K⁺ rich diets needed as a rule

Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. **Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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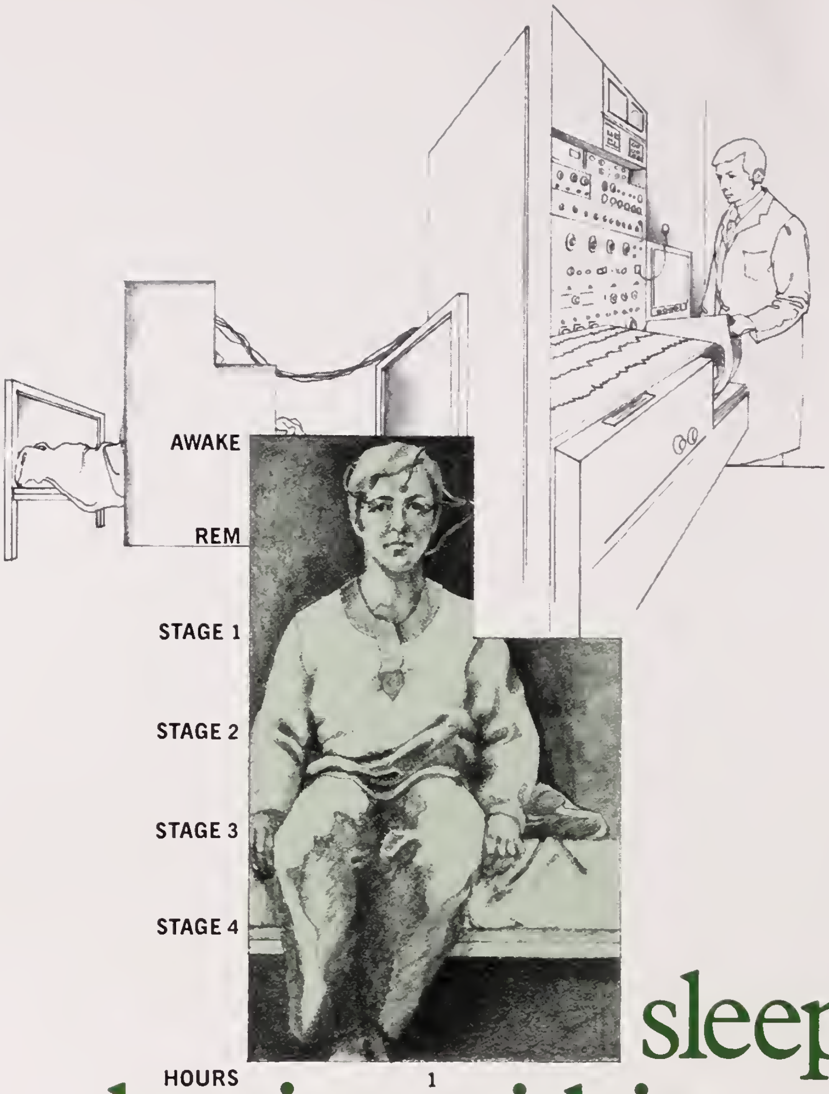
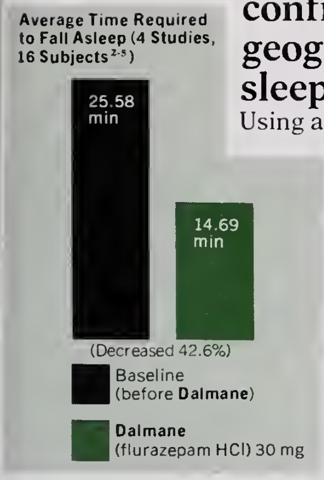


sleep begins within 17 minutes, on average... an initial benefit of

Dalmane®

(flurazepam HCl) **proved by a 22-night clinical study of insomnia patients in the sleep research laboratory and at home**[1]

Three insomnia patients selected for difficulty falling asleep were administered Dalmane (flurazepam HCl) 30 mg for 14 consecutive nights. Placebo was given for four nights prior to and four nights after Dalmane. Physiologic tracings on Dalmane nights 1-3 showed sleep induction time averaged 13.90 minutes; on Dalmane nights 12-14, 18.80 minutes. Combined average for the 6 monitored drug nights was 16.35 minutes.[1]



confirmed by clinical studies in four geographically separated sleep research laboratories[2-5]

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage[2-5]

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

Dalmane is generally well tolerated; morning "hang-over" has been relatively infrequent. While dizziness, drowsiness, lightheadedness and the like have been noted most often, particularly in the elderly and debilitated, physicians should be aware of the possibility of more serious reactions, as noted below.

Before prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

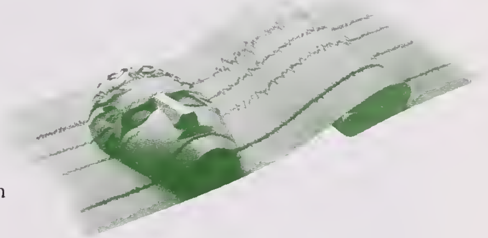
Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.



when restful sleep is indicated

Dalmane®

(flurazepam HCl)

One 30-mg capsule *h.s.* – usual adult dosage (15 mg may suffice in some patients).
One 15-mg capsule *h.s.* – initial dosage for elderly or debilitated patients.

- induces sleep within 17 minutes, on average
- reduces nighttime awakenings
- sustains sleep 7 to 8 hours, on average, without repeating dosage

REFERENCES: 1. Kales A, *et al*: *Arch Gen Psychiatry* 23:226-232, Sep 1970
2. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971
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5. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

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OUR COVER

Colorado was a place for the independent spirit. A town easily grew to too much. As it did for the prospectors who joined Dick Irwin on July 4, 1879 to leave what was then called Ute City, and later Aspen, to head for the high country where gold and silver were said to exist in unlimited quantities. In honor of the day, the town was named Independence, and though its name changed frequently during its fleeting life, we all know Independence Pass as one of the magnificent areas of Colorado. And a symbol of what we will be observing through 1976. Credit: Michael S. Kappy, MD, Commerce City, Colorado.

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Opinion & Dialogue

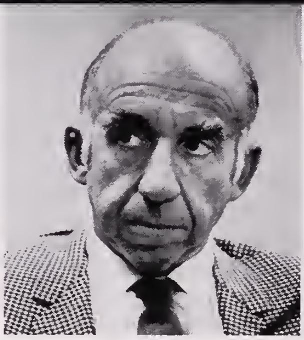
The Role of the Detail Man

Dr. Willard Gobbell
Family Physician
Encino, California

"I may be prejudiced, but I a
very much in favor of the detail m
I meet. Most of them are knowled
able about the drugs they promot
and can be a great help in acquai
ing me with new medication."

Family Physician's Perception

I think that most general practitioners in this area feel as I do about the detail man. Over the
years I have gotten to know most
the men who visit me regularly an
they in turn have become aware o
my particular interests and the na
ture of my practice. They, therefore, limit their discussion as muc
as possible to the areas of interes
to me. Since I usually see the sam
representative again in future visits, it is in his best interest to supply me with the most honest, factual, as well as up-to-date information about his products.



Dr. Jeremiah Stamler
Chairman
Department of Community
Health and Preventive
Medicine, and Dingman
Professor of Cardiology
Northwestern University
Medical School

"In the total picture of dealir
with health problems in this coun
there is a potential for detail men to play a meaningful role."

The Positive Influence

My contact with representatives and salesmen of the pharma
ceutical industry is the type of cor
tact that people in a medical cent
research people, and academic
people have and that's in all likelih
on a somewhat different level fron
that of the practicing physician.

Let me touch on how I persor
ally perceive the role of the sales representative. These men reach large numbers of health professionals. Thus they could be—and at times actually are—disseminators of useful information. They could consistently serve a real edu
cational function in their ability to discuss their products.

At present they do distribute printed material, brochures and pamphlets—some of it scientifically sound and therefore truly useful—as well as some excellent film
produced by the pharmaceutical industry. When they function in th

Is He a Source of Information?

Yes, with certain reservations. The average sales representative has a great fund of information about the drug products he is responsible for. He is usually able to answer most questions fully and intelligently. He can also supply reprints of articles that contain a great deal of information. Here, too, I exercise some caution. I usually accept most of the statements and opinions that I find in the papers and studies which come from the larger teaching facilities. It goes without saying that a physician should also rely on other sources for his information on pharmacology.

Training of Sales Representatives

Ideally, a candidate for the position as a sales representative of a pharmaceutical company should be a graduate pharmacist who has a questioning mind. I don't think this is possible in every case, and so it becomes the responsibility of the pharmaceutical company to train these individuals comprehensively. It is of very great importance that the detail man's knowledge of the product he represents be constantly reviewed as well as updated. This phase of the sales representative's education should be a major responsibility of the medical department of the pharmaceutical company.

I am certain that most of these companies take special care to give their detail men a great deal of information about the products they produce—information about indications, contraindications, side effects and precautions. Yet, although most of the detail men are well informed, some, unfortunately, are not. It might be helpful if sales representatives were reassessed every few years to determine whether or not they are able to fulfill their important function. Incidentally, I feel the same way about periodic assessments of everyone in the health care field, whether they be general practitioners, surgeons or salesmen.

Value of Sampling

I personally am in favor of limited sampling. I do not use sampling in order to perform clinical testing of a drug. I feel that drug testing should rightly be left to the pharmacology researcher and to the large teaching institutions where such testing can be done in a controlled environment.

I do not use samples as a "starter dose" for my patients. I do, however, find samples of drugs to be of value in that they permit me to see what the particular medication looks like. I get to see the various forms of the particular medication at first hand, and if it is in a liquid form I take the time to taste it. In that way I am able to give my patients more complete information about the particular medications that I prescribe for them.

capacity they are indeed useful; particularly in the fact that they disseminate broadly based educational material and serve not just as "pushers" of their drugs.

The Other Side of the Coin

Obviously, the pharmaceutical companies are not producing all this material as a labor of love—they are in the business of selling products for profit. In this regard the ambitious and improperly motivated sales representative can exert a negative influence on the practicing physician, both by presenting a one-sided picture of his product, and by encouraging the practitioner to depend too heavily on drugs for his total therapy. In these ways, the salesman has often distorted objective reality and undermined his potential role as an educator.

The Industry Responsibility

Since the detail man must be an information resource as well as a representative of his particular pharmaceutical company, he should be carefully selected and thoroughly trained. That training, perforce, must be an ongoing one. There must be a continuing battle within and with the pharmaceutical industry for high quality not only in the selection and training of its sales representatives, but also in the development of all of its promotional and educational material.

The industry must be ready to accept constructive as well as corrective criticism from experts in the field and consumer spokesmen, and be willing to accept independent peer review. The better educated and prepared the salesman is, the more medically accurate his materials, the better off the pharmaceutical industry, health professionals and the public—*i.e.,* the patients—will be.

Physician Responsibility

The practicing physician is in constant need of up-dated information on therapeutics, including drugs. He should and does make use of drug information and answers to specific questions supplied by the pharmaceutical representative. However, that information must not be his main source of continuing education. The practitioner must keep up with what is current by making use of scientific journals, refresher courses, and information received at scientific meetings.

The practicing physician not only has the right, but has the responsibility to demand that the pharmaceutical company and its representatives supply a high level of valid and useful information. I feel certain that if such a high level is demanded by the physician as well as the public, this demand will be met by an alert and concerned pharmaceutical industry.

From my experience, my impression is that sectors of the pharmaceutical industry are indeed ethical. I challenge the industry as a whole to live up to that word in its finest sense.

*Pharmaceutical
Manufacturers Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005*

P·M·A

When low back pain* interferes...

Help relieve pain, restore mobility with

PARAFON FORTE® tablets

chlorzoxazone† 250 mg ; acetaminophen 300 mg.

*This drug has been evaluated as "probably" effective for this indication.

See brief summary of prescribing information on facing page for Indications, Contraindications, Warnings, Precautions and Adverse Reactions.

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PARAFON FORTE® tablets help relieve pain, restore mobility and stop pain-spasm feedback by providing:

a nonsalicylate analgesic equal to aspirin for relief of pain,[1,2] yet unlikely to cause the gastric irritation,[2,3] allergic reactions[2] or increased bleeding time[4] associated with aspirin therapy...

and a skeletal muscle relaxant shown in extensive clinical studies to afford relief of discomfort in acute musculoskeletal conditions*[5-7] but which is not an antihistamine or tranquilizer derivative and is unlikely to produce a tranquilizing or sedative effect.[5,7,8]

***Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.
Warnings: *Usage in Pregnancy*—Use in women of childbearing potential only when potential benefits outweigh possible risks.
Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.
Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-four patients, it was not possible to state that the dysfunction was or was not drug induced.
Usual Adult Dosage: Two tablets q.i.d.
Supplied: Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 1955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, F.N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: New Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboratories, Inc.

†U.S. Patent No. 2,895,877

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When diarrhea has his number...

Lomotil puts him back in the game.

Physicians and patients both want prompt control of the symptoms of diarrhea. A rapid, uncontrolled loss of fluids and electrolytes can cause a medical crisis, particularly in children, and in patients who are seriously ill, or in people who are badly undernourished.

Lomotil usually stops diarrhea promptly. This rapid action halts the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate antibiotic therapy should be given along with Lomotil.

Lomotil has few side effects, and those that do occur are generally mild.

Lomotil®
TABLETS/LIQUID

Each tablet and each 5 ml. of liquid contain:
diphenoxylate hydrochloride ...... 2.5 mg.
(Warning: May be habit forming)
atropine sulfate .... 0.025 mg.

Usually stops diarrhea promptly.

IMPORTANT INFORMATION: This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT *AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis.

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Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

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The private and the public sector. What's in it for you?

It has been eight months since I took the "plunge" from the private sector to the public sector. While I'm sure you will not gain much practical insight from this paper, some thoughts and observations in this transition might be interesting to you. What I am to talk about is but personal observation and one man's opinion. If I sound cynical or upset at times, I can only refer to W. C. Fields' immortal statement, "If I appear to be unkind — try to understand; it's because at heart I'm really vicious."

At the present time we are confronted with the conflict between the health needs and the health wants of society. Lord Rosenheim, the distinguished British physician, once said, "Where doctors used to be summoned to deal with infectious disease, they are now increasingly expected to alleviate the effects of frustration, anxiety, and social inadequacy, to act as priests and marriage counsellors, to sense the underlying call for help in the patient with recurring backache, to help the delinquent child in the alcoholic home." We physicians were taught in our medical schools and in our hospital training to deal with the diseases found on the wards. In my view, we have been unable to cope with, or even teach about, disease as found in the community.

In medicine, as everywhere else, there have been more changes in the last five years than in the preceding fifty. This has led to confusion and disorientation. In Alvin Tofler's *Future Shock,* he has said that this translates into a "decisional crisis" in which organizations, of which we are all a part, are given little time to confront new problems. These are problems that require creative, innovative responses, and the old processes of decision-making leave us unequal to the task. There just isn't time to sit down and cogitate. If you do, the new problems are on you before the old ones are solved. Try my job for one day and you will see how true it is.

These changes and their frustrations are reflected in the semantics of any medical discussion these days. How do we get along with the changing regulations of the government, being caught as we are in the web of regulations, dis-trust, and outright viciousness against the medical profession by the government and its representatives? We now have the awkward acronyms, HMO's, PSRO's, NHI. Is there any physician who has not run afoul of some regulation, be it Medicaid, Medicare, or the rest? Has not each of us grappled with one technical error on some chart that has taken precious time away from the care of the patient? And where is the leadership to help us? Unfortunately, "future shock" is on us, too, and on the medical leadership at all levels, in both the public and private sectors.

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*From a presentation before the Colorado Society of Internal Medicine. Oct. 1974. From 1946 to 1974 Dr. Kauvar had a distinguished career in the practice of internal medicine in Denver. In 1974 he accepted appointment as Manager of Health and Hospitals, Denver.

But, there are some encouraging aspects to this problem. Medicine is becoming more unified and more realistic. The private practitioner and the hospitals, be they public or private, are developing an amalgam and working relationship that bodes well for the future. Since Hippocrates' time the ethical values of medicine have been the "science of human biology and its application to suffering humanity by the art of clinical medicine." Science has to include the most elaborate experiments in molecular biology, up to and including behavioral observations of the whole man and groups of people. The Art of Medicine must range from the bedside practitioner — a physician conduit based on a concern for the patient and the family — up to and including the most minute subspecialty. The science and the art must be practiced together to bring merciful care to the sick.

We are now, for the first time, evaluating what primary health care means and doing something about it. The content of this program can be spelled out as follows — and this is one man's opinion, although others, like Dr. Charles Janeway, have expressed it earlier:

1. **Management of Acute Emergencies.** The doctor is really the only one of the health team who can be trained to take the course of action on which life depends.

2. **Early Detection of Serious Disease.** We have adequate methods of treatment for many diseases, but recognizing them and taking care of them early is the physician's responsibility. Recognizing appendicitis, pyogenic meningitis, spinal cord tumor, or even cancer early can save untold harm.

3. **Identification of Individuals at Special Risk.** Examples are erythroblastosis from RH sensitization, diabetes, drugs, alcohol, and the development of mental retardation from phenylketonuria.

4. **Health Frustration.** This category includes genetic counseling, family planning, growth and development, trauma and the environment.

5. **Ability to Aid the Chronically Ill with Continuous Care.** As more of our people are getting older this is a growing responsibility. It poses a serious organizing problem with which we at Denver General are vitally concerned, as is the private sector, for example, the Denver Clinic Foundation.

The hospital is taking its rightful place in a health-oriented community. The public hospital has been the mainstay and the resource site, but the private hospitals are coming on fast. In an article entitled, "The Hospital," Dr. John H. Knowles stated: "Perhaps the most profound and promising development in the evolution of the American hospital has been its gradual emergence as a health center, although this potential is far from being realized. The hospital is no longer solely a passive, acute, after-the-fact curative institution. Through the developing emergency wards, social service departments, and ambulatory clinics, through liaison with extended care facilities, nursing homes, clinics, hospitals, and home care services, and through the establishment of neighborhood centers, it has extended its interests actively to the community in the interests of keeping down costs, reaching more people in need, and preventing, or at least containing, illness."

Denver and its Health and Hospitals has been a leader in this field. We were the first in the country and have maintained our leadership, although many practicing physicians have never been into one of these Neighborhood Health Centers. Suffice it to say that one-quarter of all the people seen at the neighborhood health centers have never seen a doctor in their lives. Following the establishment of this program the infant mortality dropped from a high of 24.7 per cent in the target areas we serve to a level that is the same all over the city — rich or poor. For the first time, at one office, a patient can receive total care, be it mental or physical health, nutrition, legal aid, or social service. It is my fond hope that the next neighborhood health center will be opened by the private sector via one of its hospitals. Why not? There are so many advantages for both the public and private that it will serve as a unifying point. The physicians we have in the neighborhood health centers are the ones that would be looking for fulfillment in the missionary hospitals of old, in Project Hope, or in the Peace Corps. All of us still have a little of the idealism that we once had in abundance when we started medical school.

Finally, from the vantage point that I have been fortunate to have, I can look at the vast changes in medicine in relationship to the consumer public and see how this can be channeled for good.

Howard Hiatt, the distinguished Internist, and now Dean of the Harvard School of Public Health, tells the story of a first-year Harvard medical student who came into his office and berated him. As he tells it, "How could we justify," she demanded, "the enormous expenditure of society's resources for the care of the large number of elderly patients hospitalized for treatment of advanced degenerative disease, when just a few minutes walking distance from the hospital there were hundreds of children with inadequate diet, housing, and medical care?" Two years later, on the first day of this doctor's clerkship, Dr. Hiatt saw her emerge from a patient's room. When asked how the day had gone, tears welled up in her eyes. Her first patient had been a man in his 80's, confused, paralyzed as a result of a stroke. This was her first personal exposure to the problem she had posed to him two years earlier, and the shoe was on the other foot. However deeply she felt about her previously expressed opinions of the inequities in society's resources, as one patient's physician she could focus only on his needs and what was best for him.

Isn't this the dilemma we are all in — our responsibility to the health needs of the individual and yet to a larger degree the health of society? In a world that tends to allow problems to be pigeon-holed, the physician has been responsible for both the individual and the society's health problems, although he is primarily trained for only the first. But it is the second that I see the public sector hospitals as being able to do the greatest good. The private physician, caught up in the ever-demanding care of individual patients, has little time to step back and appreciate, much less change, the inefficiencies of a system which has never been given consideration.

It is the duty and must be the desire of the Health and Hospitals Agency of the City, and its Director, to be involved in alcoholism-crime, child abuse, mental health, inadequate housing, the environment, faulty sanitation, and on and on, as it applies to health care. It is the duty of this sector to work with all levels of society, be it consumers, politicians, private practitioners, medical educators, to find the answers to these most difficult questions. By being leaders in this neglected field of medicine, we can aid all the physicians in their public and private image. By doing this and working with others, not only will the physician have innovative approaches, and hopefully earlier solutions, but the practicing physician will be much freer to attend to his primary concern, the care of his patient.

This I have pledged myself to do.

A. J. Kauvar, MD, Denver

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Roentgenologic features

*In treatment of respiratory distress syndrome**

Virgil B. Graves, MD, Great Falls, Montana

Roentgenologic examination of the chest has become increasingly important in early diagnosis and clinical care of infants with Hyaline membrane disease (HMD) or as it has been called more recently, respiratory distress syndrome (RDS). The new and vigorous approach to neonates and premature infants with RDS and with other respiratory diseases has brought about development of infant intensive care units. These units have extended the uses of incubators, umbilical vascular catheterization and respirators in the clinical care and management of infants with RDS and respiratory diseases. These procedures and treatment modalities are associated with several significant roentgenologic findings (Table 1) which the physicians must recognize and correctly interpret.

Pseudocyst Artefact

Roentgenogram of an infant examined through a plastic incubator may show an artefactial cyst-like structure produced by the holes in the plastic incubator. Due to positioning of the infant this may produce radiographic findings not unlike those of a cyst in the abdomen or lungs. (Fig. 1) The proper diagnosis can be made if one notes that the cyst appears exceptionally discrete and radiolucent.[1] Also, as in this example, the pseudocyst may extend outside the confines of the infant's body.

Umbilical Vessel Catheterization

Catheters can be placed either in the venous or arterial systems through the umbilical cord. The radiographic features of normal catheter placements have been described[2-4] and are illustrated in Fig. 2 and Fig. 3. Figure 2A is the initial film of this infant and shows rather classical changes of RDS and a normally positioned umbilical arterial catheter. Deviation from these positions would suggest an abnormal catheter placement. Recently a distinct trend to arterial catheterization has developed because of complications with venous catheterization and because of need for arterial oxygen monitoring.[5,6] There are differing opinions as to the proper placement of the arterial catheters. Some advocate the placement of the catheter in the mid thoracic aorta, above the celiac axis, and others prefer placement at or near the common iliac vessels.

In many instances, the catheter may enter the portal systems, superior vena cava, cross a patent foramen ovale entering the left atrium or pulmonary veins (Fig. 4), or cross the tricuspid valve entering the right ventricle, pulmonary

TABLE 1

ROENTGENOLOGIC FINDINGS ASSOCIATED WITH THE COMPREHENSIVE MANAGEMENT OF RDS.

1. Artefacts produced by incubators:
    Pseudocyst.
2. Umbilical vessel catheterization:
    Placement.
    Complications.
3. Respiration changes:
    Intrapulmonary interstitial emphysema (IIE)
    Pneumothorax.
    Pneumomediastinum.
    Bronchopulmonary dysplasia.

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*From the Department of Radiology, Columbus Hospital, Great Falls, Montana.

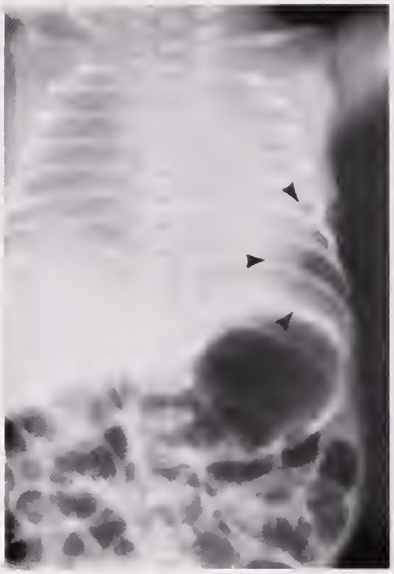

Fig. 1. PSEUDOCYST ARTEFACT: Cyst-like structure (arrows) over the left lower lung is an artefact produced by a hole in the plastic top of the incubator. Also note the appearance of the umbilical venous catheter.

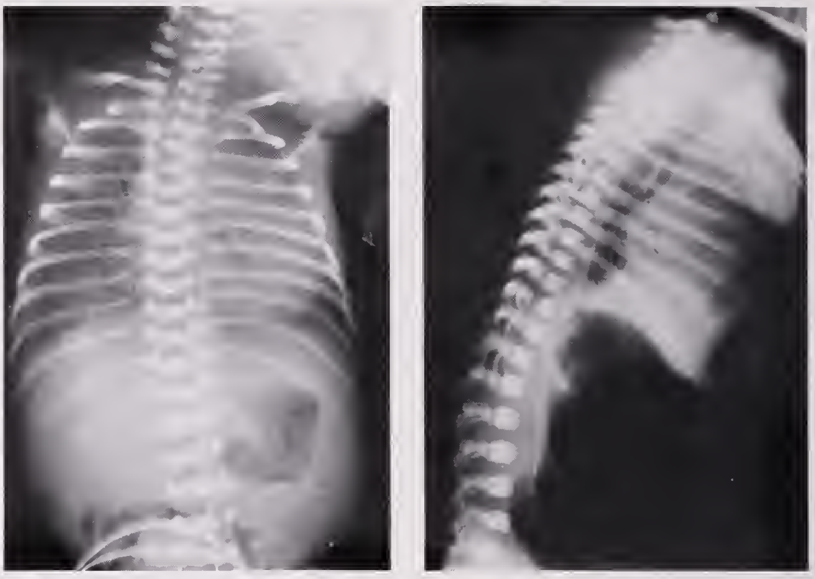

Fig. 2. NORMAL UMBILICAL ARTERIAL CATHETER POSITION: A and B demonstrate the normal positions of the arterial catheter on frontal and lateral views. The catheter passes from the umbilical artery downward to the iliac vessels and then upward into the aorta. The distal tip is located within the thoracic aorta.

artery, or patent ductus. Many complications of umbilical vessel catheterization have been reported and are listed in Table 2.

Respirator Complications

Complications such as air trapping, intrapulmonary interstitial emphysema (IIE), pneumothorax, pneumomediastinum, and bronchopulmonary dysplasia were not considered to be common features of RDS until the institution of respirator assisted therapy. This treatment would appear to be a causative factor. Certain newborns with RDS appear to have a high risk of developing a pneumothorax. A roentgenologic feature, IIE[18] has recently been described and may precede the development of a pneumothorax. Physicians aware of this finding may be able to critically predict which newborns with RDS are at risk to develop a pneumothorax.[19] Development of IIE and a subsequent pneumothorax on a followup film 20 hours later are illustrated by Fig. 5: A, B, and C.

Northway[20] described bronchopulmonary dysplasia, a complication of infants with RDS, treated for more than 24 hours with 80-100% oxygen and intermittent positive pressure respirator therapy. The radiographic findings of bronchopulmonary dysplasia are multiple small rounded areas of radiolucency distributed throughout both lungs within a reticular framework, producing a picture very much like a sponge (Fig. 6). All of the changes in

TABLE 2

COMPLICATIONS OF UMBILICAL VESSEL CATHETERIZATION

1. Vascular perforations
2. Perforation of the heart with cardiac tamponade[7]
3. Breaking of catheter with embolus[8]
4. Intestinal perforation[9,10,11]
5. Peritoneal cavity perforation[12]
6. Arteriovenous fistulae[13]
7. Thromboembolism[5,14]
8. Hemorrhage from catheter if separated or dislodged
9. Hepatic abscess[15,16]
10. Buttock necrosis[17]
11. Sepsis
12. Transitory blanching or loss of distal pulses of the lower extremities[17]

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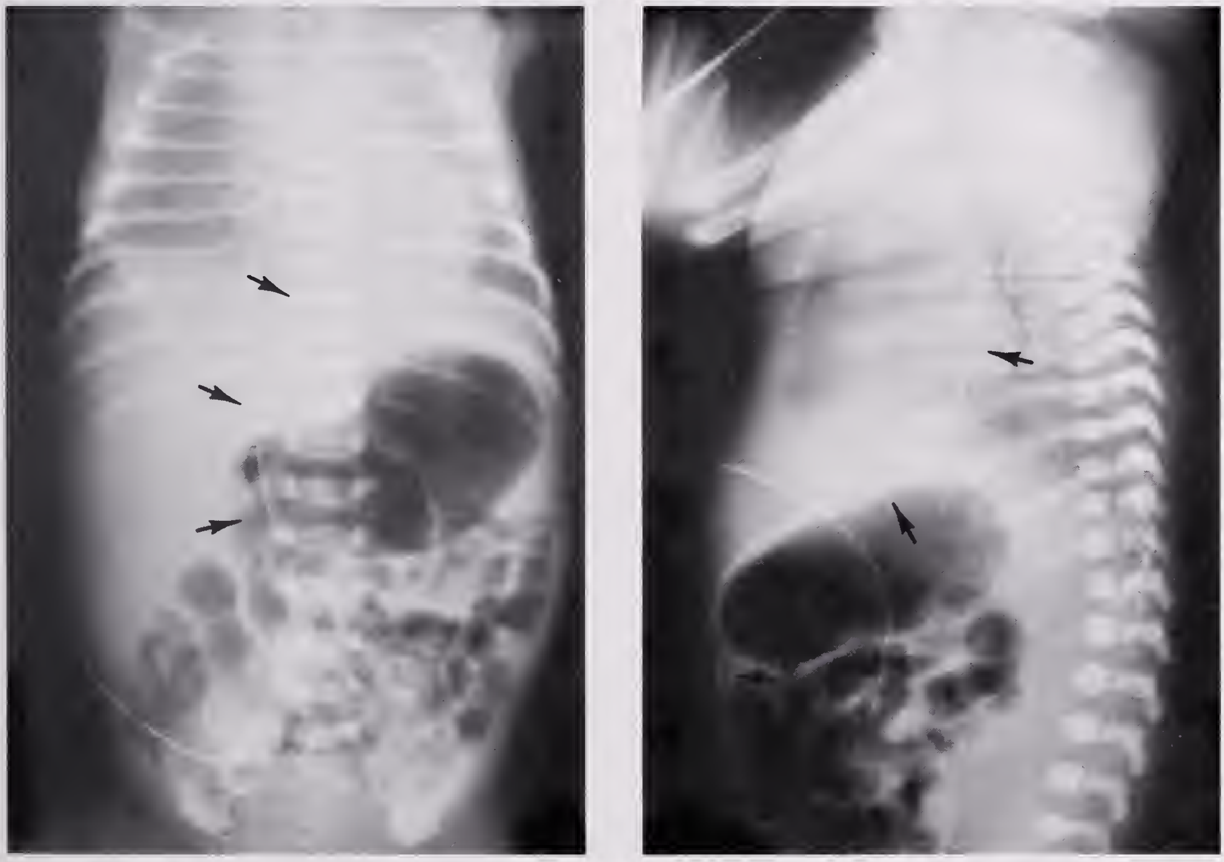

Fig. 3. NORMAL UMBILICAL VENOUS CATHETER POSITION: A and B demonstrate the normal course of an umbilical venous catheter. Note the gentle curve on the frontal film (arrows) which is a feature of venous catheterization. Normally on the lateral view (B) the venous catheter passes through the ductus and then makes a smooth upward curve and terminates posterior to the heart in the inferior vena cava. Any deviation from this should suggest abnormal placement (see Fig. 4)

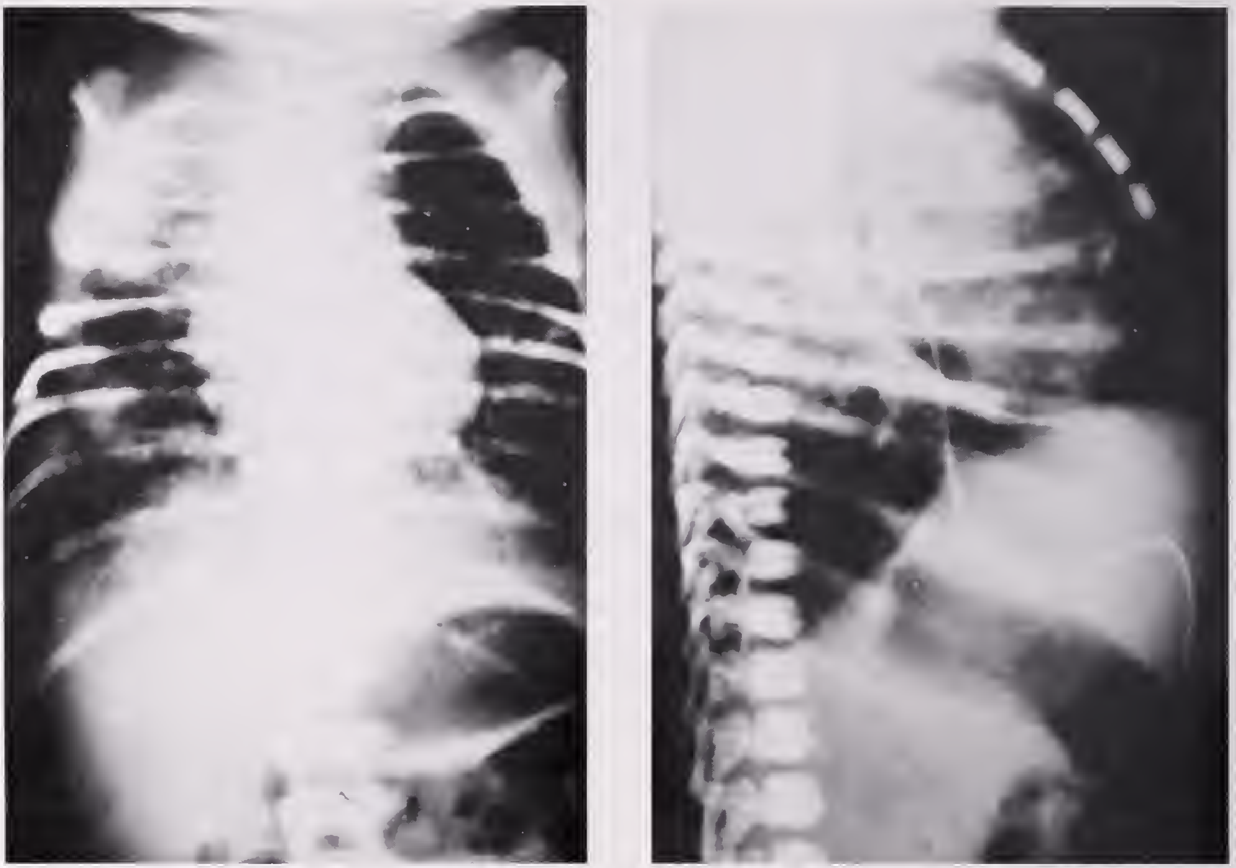

Fig. 4. ABNORMAL VENOUS CATHETER POSITION: Note that the catheter passes through the ductus into the inferior vena cava and right atrium, then courses across a patent foramen ovale to terminate in the left atrium.

bronchopulmonary dysplasia probably result from capillary wall damage and micro hemorrhage. The causative factors appear to be prolonged exposure to high oxygen concentration[21-23] or respirator assisted breathing[24-26] or a combination of both.

Discussion

Many reports have established the usefulness of vigorous and comprehensive treatment of the acutely ill, high risk, newborn infant with RDS. These treatment regimens make use of incubators, arterial oxygen monitoring, supplemental oxygen, positive pressure respirator assisted breathing, and the administration of buffering agents and fluids through an umbilical catheter.

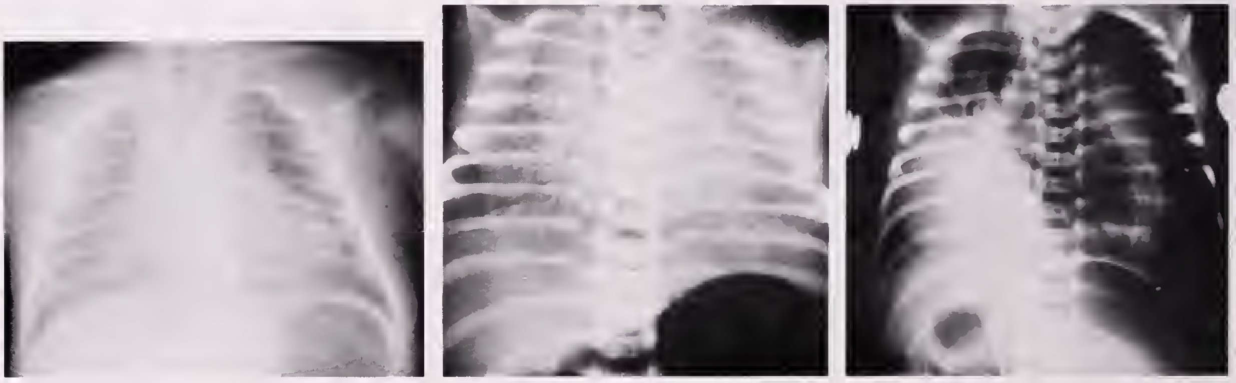

Fig. 5. INTRAPULMONARY INTERSTITIAL EMPHYSEMA (IIE) WITH PNEUMOTHORAX: A. Initial chest film of an infant with RDS. B. Followup chest film shows the development of IIE. Both the linear and cyst-like radiolucencies are well demonstrated. C. Shows a followup film made 20 hours after (B) with the development of a pneumothorax. Note the normal position of umbilical arterial catheter in (B) and (C).

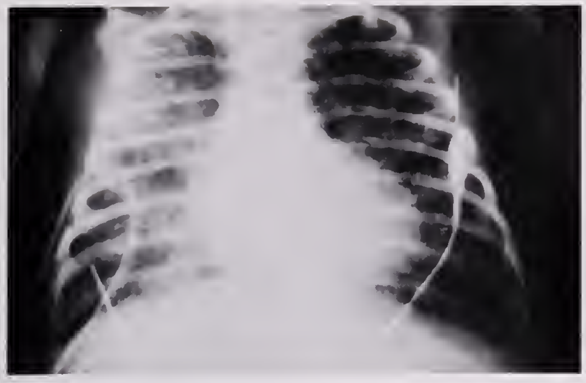

Fig. 6. BRONCHOPULMONARY DYSPLASIA: This AP chest was made following sustained respirator and oxygen therapy. The radiographic picture of bronchopulmonary dysplasia is well demonstrated.

While these methods have proven useful, and mortality rates have decreased, the risk is significant. The physicians involved in this type of comprehensive care must be aware of the possible complications and clinical course associated with their use. Because of this, the chest roentgenograms have become increasingly important in the diagnosis and clinical management of these infants. The roentgenologic findings associated with the comprehensive treatment of RDS must be recognized and interpreted correctly. •

ACKNOWLEDGMENT

Special thanks to Lenord Swischuk, M.D., U.T.M.B., Galveston, Texas for the case illustrated in Fig. 6.

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Alkaptonuria

A Case Report

Elton J. Adams, MD and John R. Ward, MD, Salt Lake City

THE ETIOLOGY OF OSTEOARTHRITIS is unknown but generally occurs in older patients. When seen in patients under 40 years of age, underlying diseases such as hemochromatosis, acromegaly, trauma, or other causes of joint damage are usually present. Alkaptonuria is also a cause of osteoarthritis. It is a rare inherited metabolic disorder characterized by the classic triad of hemogentisic aciduria, ochronosis, and arthropathy. Over the past century, approximately 100 patients have been reported in the American literature and 500 cases in the world literature. The purpose of this paper is to report the first patient with ochronosis that we are aware of in the intermountain area and to briefly describe the clinical features of this disease.

CASE REPORT

A 33-year-old white male from Idaho gave a history of low back pain of at least 10 years duration. Eight years prior to admission he injured his back with symptoms suggesting disc involvement. A myelogram was considered at this time but not performed. The back pain slowly progressed and he also noted aching in his hips. He had never been aware of dark urine, but he had noted that his cerumen was black. There was no family history of arthritis, and his parents were not blood related.

Pertinent physical findings showed a faint bluish pigment of the ear cartilage which on transillumination of the ear appeared opaque and gray (Fig. 1). Tympanic membranes were slightly discolored at their periphery and the cerumen was "jet black." Small brown pigmented areas were noted over the lateral sclerae (Fig. 2). There was loss of lumbar lordosis with decreased range of motion of the lumbar spine and pain on flexion, extension, and lateral movement. Peripheral joints were normal with the exception of pain and decreased range of motion of the left shoulder. Routine laboratory tests including sedimentation rate were within normal limits. The urine which was normal in color when freshly voided became black on standing overnight or with the addition of 1 N NaOH (Fig. 3). X-ray of the spine showed the characteristic chondrocalcinosis of the intervertebral disc spaces (Fig. 4).

Discussion

Alkaptonuria is a metabolic disease transmitted by a single recessive autosomal gene in which there is a complete deficiency of the enzyme homogentisic acid oxidase.[1,2] As a result of this deletion there is an accumulation of homogentisic acid (a normal intermediate in the metabolism of phenylalanine and tryosine) which is excreted in the urine (Fig. 5).

Ochronosis is the condition in which there is deposition of brown-black pigment derived from polymerized homogentisic acid in the connective tissue usually apparent clinically in cartilage of ear, skin and sclera. Patients with alkaptonuria who live to the fourth decade of life almost invariably develop ochronosis. The common extra-articular soft tissue sites of ochronosis include the skin, eye, ear, cardiovascular structures, and genitourinary tract.

Of the clinical symptoms of ochronosis the most important is the arthropathy. It is postulated that the oxidized polymers of homogentisic acid in some way inhibit the enzyme systems involved in cartilage metabolism. As a result normal resiliency is lost and this tissue becomes brittle and fibrillated. Minute fragments of this abnormal cartilage are broken off and displaced into the synovial tissue where they may evoke a foreign body reaction and the formation of new bone tissue, osteochondral bodies. The end result is an accelerated degenerative process in cartilage leading to a progressive arthropathy which usually follows a consistent pattern. Back pain and stiffness begin when the patient is in his 30's; during the next ten years the knees become involved, and later the hips and shoulders. The course is chronic and progressive, and by 60 years of age the patient may be totally incapacitated. In males, joint involvement occurs more frequently, develops at an earlier age and is of greater severity than in females. The first manifestation in 20 per cent of males with ochronotic spondylosis was an acute rupture of a nucleus pulposus usually in the 20's. Disc syndromes are rare in women. The earliest site of spondylosis is in the lumbar spine with the cervical and thoracic spines becoming involved later. Stiffness of the low back progresses to rigidity and loss of lumbar lordosis. The typical posture and gait of the patient with ochronotic spondylosis is quite similar to that of the patient with ankylosing spondylitis.

Involvement of peripheral joints occurs several years after spondylosis. The knee is the most frequently affected peripheral joint. Symptoms may be acute or insidious in onset and consist of pain on weight bearing or stiffness. As the disease progresses, range of motion becomes restricted and flexion contractures may develop. Synovial effusions are quite common in affected knees and often follow negligible trauma. Symptoms of hip and shoulder involvement are usually milder than knee. The small joints of the hands and feet are spared in ochronosis.

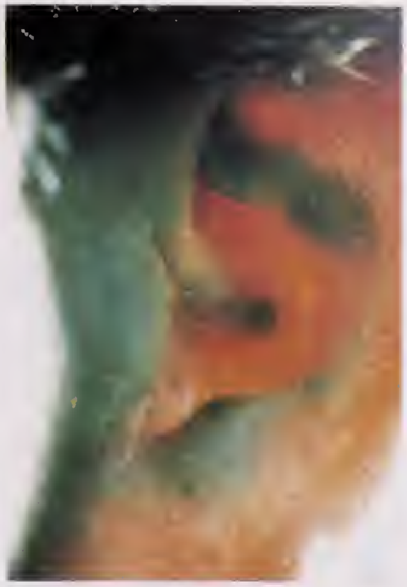
Fig. 1. Transillumination of the left ear showing the pigmented ear cartilage which appears opaque and gray.

In the skin, pigmented granules are found in the dermis as well as sweat glands. In advanced cases a faint brownish or bluish hue may be found in the malar areas of the face and in the axilla and groin. Sweat may be discolored and stain clothing brown.

Ochronotic pigment may be deposited in any of the outer structures of the eye including sclerae, cornea, conjunctivae, tarsal plates, and eyelids, and the changes in the sclerae occur relatively early and many years before arthropathy develops. One of the early physical signs of ochronosis is a bluish discoloration of the ear cartilage usually readily visible by the fourth decade. In addition to the striking lesion of the external ear the other "earmarks" of ochronosis include black cerumen, discoloration of the tympanic membranes, and deafness.

Cardiovascular lesions include pigmentation of the heart valves, endocardium and the intima of the aorta. In 51 cases of clinically documented ochronosis, one half had evidence of cardiac abnormalities including cardiomegaly, organic murmurs, abnormal electrocardiograms, and roentgenograms of the chest. At one time it was felt that ochronosis accelerated arteriosclerosis, however the prevalence of arteriosclerosis in well studied cases is no greater than in the general population.

Genitourinary complications are common in patients with ochronosis. Prostatic calculi are frequently found in males. Apparently the alkaline secretion of the prostate promotes rapid polymerization of homogentisic acid and this pigment then forms a nidis for a stone. Renal stones occur and recur in ochronosis usually in the fifth and sixth decades. The stones are black, porous, and may attain large size. Clinically apparent renal disease does not occur from the deposition of ochronotic pigment in the renal parenchyma.

The diagnosis of alkaptonuria is not difficult. Freshly voided urine is normal in color and on standing slowly turns brownish-black as the homogentisic acid is oxidized. However, most patients are unaware that their urine will darken on standing. If NaOH is added to fresh urine, the homogentisic acid is oxidized and the urine

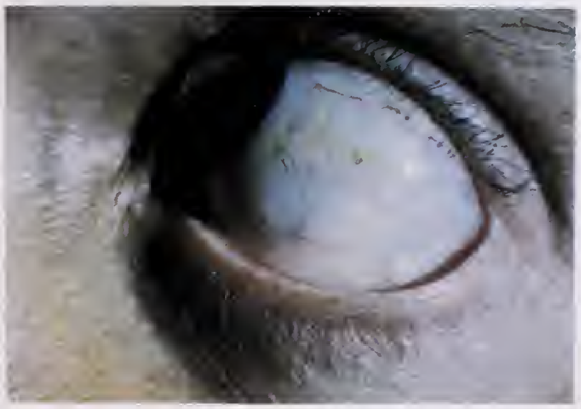
Fig. 2. Deposition of ochronotic pigment in the lateral sclera.

promptly turns black. Homogentisic acid also reduces the copper in Benedict's reagent giving a yellow-orange precipitate which is usually misinterpreted as indicating glucosuria. Using clinitest tablets a black supranatant may be seen.[3] An enzymatic method for determining homogentisic acid in urine and blood is available. Normal urine contains no homogentisic acid.

The characteristic pigmentation in connective tissue suggests the diagnosis. The x-ray appearance is classic and establishes the diagnosis of ochronotic spondylosis. The principal feature is the appearance of calcific deposits in the intervertebral discs. There is presently no means of detecting heterozygotes. Thus, the diagnosis of alkaptonuria and ochronosis needs only to be thought of to be made.

Attempts to treat alkaptonuria have been directed toward correcting the underlying metabolic defect or preventing or reversing pigmentation and arthropathy. Reduction of dietary phenylalanine and tyrosine over a long period is not practical; however, one report has indicated that two patients experienced decreased arthritic symptoms on such a diet. Ascorbic acid, which reduces oxidized homogentisic acid in vitro, does not reduce the 24-hour urinary homogentisic acid excretion levels in patients with alkaptonuria. However, it has been shown that ascorbic acid reduces the amount of binding of oxidized homogentisic acid in connective tissue of rats with experimental alkaptonuria.[4] It remains to be demonstrated whether high doses of ascorbic acid particularly in the younger patient might inhibit deposition of ochronotic pigment. Over the years a variety of other agents have been tried without influence on the metabolic deficiency. Thus, treatment is primarily symptomatic and is aimed at relief of pain and prevention of deformities. Surgical removal of osteochondral loose bodies is warranted when they interfere with motion.

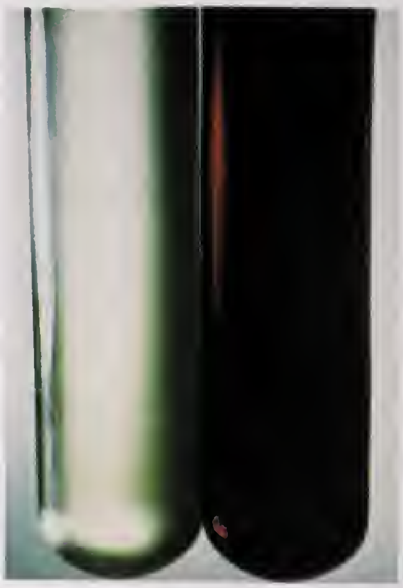

Fig. 3. Freshly voided urine is normal in color. When 1 N NaOH is added, the urine turns brownish-black.

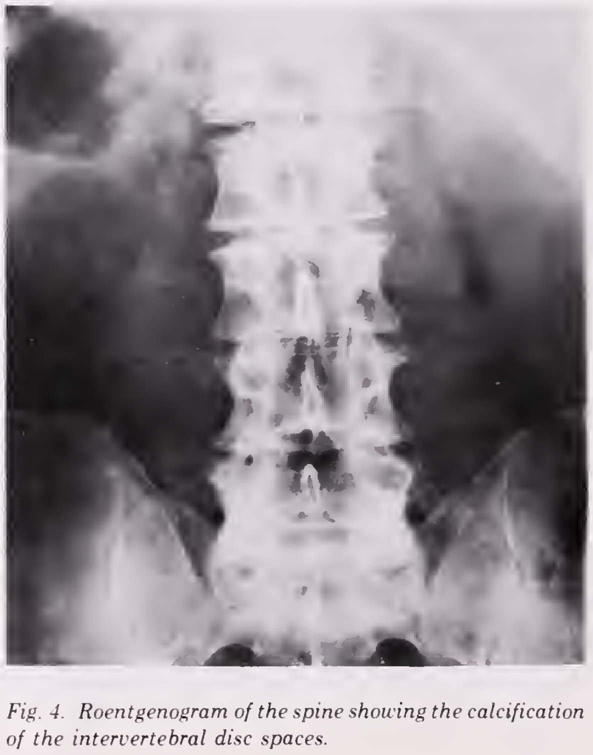

Fig. 4. Roentgenogram of the spine showing the calcification of the intervertebral disc spaces.

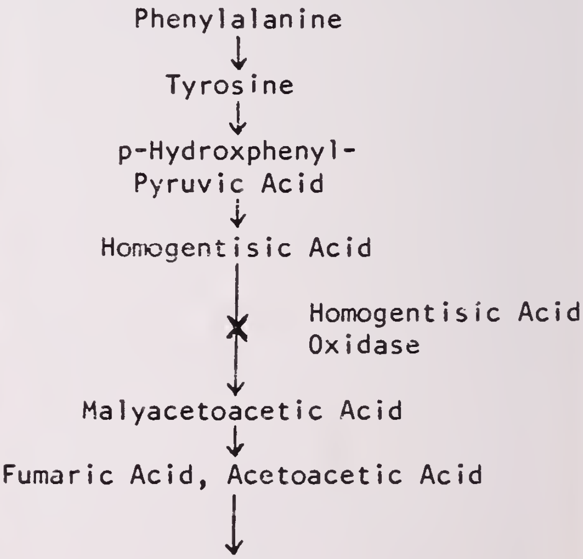

Fig. 5. Schema of pathways involved in the metabolism of phenylalanine and tyrosine indicating the block in the oxidation of homogentisic acid in alcaptonuria.

It now seems probable that alkaptonuria is less rare than was believed 30 years ago. A study from Northern Ireland reported the prevalence at 3-5 per million individuals and this would place the incidence of heterozygotes much higher than previously assumed. This means that many cases of ochronosis are not detected. This is understandable since most patients are not aware of dark urine, the physical findings may be subtle, and degenerative arthritis is a common ailment.

Physicians should become more aware of this disease and in particular should consider the diagnosis in the following situations: (1) ruptured disc in a young male, (2) premature degenerative arthritis, (3) in the differential diagnosis of dark urine, (4) false positive test for glucosuria.

ACKNOWLEDGEMENT

We would like to thank Dr. Donald Bjornson for referring this patient, and The Upjohn Company for partial support of this paper.

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Fellowships Established

Establishment of the Edwin L. Crosby Memorial Fellowships for "persons who display the breadth of vision and sense of mission that distinguished Edwin L. Crosby, MD" has been announced by the Hospital Research and Educational Trust, Chicago.

Doctor Crosby served as chief executive officer of the American Hospital Association and the Trust, an affiliate of the Association, from 1954 until his death in 1972. Each six-month fellowship award in his memory will total $9,000, to be allocated on the requirements of the individual project and the circumstances of the candidate. Funds derive from a memorial fund set up by the Trust.

Selection of fellows is to be based on such criteria as quality, timeliness, and potential usefulness of a proposed problem-solving project, the background and potential of the candidate as investigator and/or as an administrator of a health care institution or organization.

Application deadline is March 1, 1975. For further information, write: Director, Hospital Research and Educational Trust, 840 North Lake Shore Drive, Chicago, Illinois 60611.

Iatrogenic hematometra

Cryogenic corking of the cervix: Case report

Charles E. Galt, MD, Carlsbad, New Mexico

The literature is rife with allusions to profuse vaginal discharge subsequent to cryoconization of the uterine cervix. The following experience is reported as one of an opposite nature.

An 18-year-old para two, 8 weeks postpartum, with extensive cervicitis was treated with a cryogenic probe at −65°F. for 3 minutes, then permitted spontaneous thawing. She presented herself at the emergency room on the morning of the second day following treatment, approximately 42 hours post-freeze, complaining of incapacitating lower abdominal pain. She appeared very uncomfortable. Her vital signs were normal, and there was neither nausea nor diarrhea. The lower abdomen was tender and tense, but not distended or rigid. There was neither rebound tenderness nor "psoas" sign. She was given meperidine hcl, 50 mg and phenergan 25 mg intramuscularly, plus a prescription for a ½-grain codeine oral compound. She appeared in the office approximately 5 hours later, denying any degree of relief. More as ritual than with an idea of visualizing a causative factor, a speculum was introduced into the vagina, revealing the large, greenish-white concavity, representing the post-frozen cervix, but no sign of external os. This orifice was rather easily located and identified with a Bozeman dressing forceps, which instantly released a gush of "old blood" in an amount estimated at a tablespoonful or 15cc. The patient returned the following day, entirely free of complaints, and has so remained since.

References in the literature mention post-freezing edema, partial obstruction of the cervix, and occasional long-range stenosis as complications of cryoconization. None includes such an acute, severe, symptomatic, mechanical complication of the procedure as presented here. In the absence of histologic investigation into this episode, one could speculate the blockage of cervix resulted from edema rather than agglutination by healing process. The symptoms occasioned by this development were not those usually attributed to the procedure.

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Hypercalcemia with ovarian granulosa cell carcinoma

Peter M. Cannon, MD, Charles R. Smart, MD,
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Hypercalcemia most often is associated with hyperparathyroidism or neoplasms with metastatic bone disease. More rarely, hypercalcemia is related to tumors producing parathyroid-like hormone. An unusual case of hypercalcemia associated with recurrent ovarian granulosa cell carcinoma is presented. The patient had subtotal parathyroidectomy, but only after excision of the ovarian carcinoma, did the serum calcium return to normal.

Hypercalcemia is recognized as an important manifestation of serious underlying disease such as hyperparathyroidism, sarcoidosis, vitamin D intoxication, milk alkali syndrome, and neoplasms including multiple myeloma,

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lymphoma, metastatic disease, and tumors producing parathyroid-like hormone. Anorexia, nausea, vomiting, apathy, and coma may result from hypercalcemia and are not specific symptoms of the underlying abnormality, hence the importance of a systematic search to determine the etiology of the hypercalcemia.[6]

Hypercalcemia may be associated with many types of tumors. Woodard[14] in reviewing 135 patients with neoplasms (multiple myeloma excluded) found elevated serum calcium in 8.9 per cent. It is well known that breast carcinoma has a tendency to produce osteolytic metastases and subsequent hypercalcemia. In addition, there are other tumors without evident osteolytic lesions on X-ray examination that may produce hypercalcemia, including neoplasms of the lung, kidney, pancreas, ovary, as well as lymphoma.[2,7] As early as 1941, Albright suggested that these tumors may secrete a parathyroid-like hormone.[4]

Ovarian neoplasms are not a common source for ectopic hormone production. However, Cushing's syndrome,[12] hypoglycemia,[11] hemolytic anemia,[10] and hypercalcemia[13] have been reported in association with ovarian tumors. Ferenczy,[5] et al., in a review article, noted fourteen cases of ovarian carcinoma with hypercalcemia. Serous cystadenocarcinoma and mesonephroma had the highest incidence and other malignancies included dysgerminoma, undifferentiated carcinoma, and a malignant lipoid cell tumor. In this review there were no cases of granulosa cell carcinoma.

Case report of a patient with recurrent ovarian granulosa cell carcinoma which proved to be the cause of hypercalcemia follows.

CASE REPORT

A twenty-five year old white gravida four, para four markedly obese housewife, weighing 295 pounds, 5 feet 4 inches tall, entered the Latter-Day Saints Hospital in September, 1971, complaining of abdominal pain, nausea and vomiting. The patient had been explored in December, 1969, at another hospital for persistent lower abdominal pain and a questionable right adenexal mass. A tumor of the right ovary measuring 16 x 15 x 10 cm was removed with the right salpinx. Histologic diagnosis was granulosa cell carcinoma. More extensive surgery or radiation therapy was recommended, but she refused further treatment.

Ten months later, because of recurrent lower abdominal pain, the patient underwent abdominal re-exploration. There was no evidence of metastatic disease, but the normal left ovary and tube were removed. A hysterectomy was not done because of her extreme obesity. Serum calcium was normal at 9.7 mg%.

She was re-admitted in September, 1971, with weakness, extreme nausea, and vomiting. The serum calcium was 18.6 mg% (normal 8.9-10.1) and the serum phosphorus was 2.4 mg% (normal 2.4-4.2). A thorough complete evaluation disclosed normal findings on chest X-ray, IVP, bone survey, liver scan, and Pap smear. X-rays of her hands showed no subperiosteal resorption, and the lamina dura was intact. An IV phosphate infusion was given and the serum calcium was lowered to 10.4 mg%. The serum phosphorus increased to 5.2 mg%. Over the next several days the serum calcium returned to the previous high values. Serum parathormone (PTH) was 304 Pg/ml (normal 255 Pg/ml, S.D. 82 Pg/ml). This was elevated when considered in association with her elevated serum calcium. Blood urea nitrogen and serum creatinine were normal, but urinary estrogens were elevated in spite of her previous bilateral oophorectomy.

The possibility of a functioning parathyroid adenoma was suspected and neck exploration was performed September, 1971. Four normal-appearing parathyroid glands were biopsied, histologically confirmed, then a subtotal parathyroidectomy of three and one-half glands was performed. The superior mediastinum was explored, without division of the sternum, but no other parathyroid tissue was identified. Following surgery, she remained hypercalcemic, even though oral phosphate and steroids were given.

Radiation therapy was considered but not given because of her extreme obesity and insufficient evidence for recurrent ovarian carcinoma. A pelvic examination under anesthesia showed no masses and was followed by a dilatation and curettage which revealed secretory endometrium. She was then given nitrogen mustard because the clinical impression was that she might have recurrent ovarian tumor. This treatment had little effect on the serum calcium level.

In November, 1971, the patient was re-admitted with recurrent nausea, vomiting, and a serum calcium of 17.0 mg%. At this time, a mass was palpable in the lower abdomen. Exploration was done for probable recurrent granulosa cell carcinoma. A two-thousand gram granulosa cell tumor arising in the right broad ligament was found and removed. There was no evidence of liver or other organ involvement. Postoperatively, her serum calcium dropped to normal. At the time of release from the hospital, the serum calcium was 7.0 mg%.

In December, 1971, chemotherapy was begun with oral chlorambucil, which has been continued. On January 24, 1972, external cobalt-60 treatments were given to the pelvis; 5,000 rads were administered over a five-week period. At the beginning of the radiation therapy, the patient's serum calcium was 10.0 mg%.

She was readmitted in April, 1973, because of abdominal pain and vomiting. Her serum calcium was 5.4 mg%. Abdominal X-ray indicated a small bowel obstruction. An oral cholecystogram showed a single non-opaque gallstone. Exploratory laparotomy showed no recurrent ovarian tumor. Many adhesions were present around the terminal ileum, so an ileo-transverse colostomy was done to bypass the area of obstruction. Also a cholecystectomy was done.

The patient continues to have no evidence for recurrent ovarian tumor. She is doing well except for mild diarrhea. In September, 1973, the serum calcium was normal at 9.5 mg%.

Discussion

Granulosa cell ovarian carcinomas comprise 0.6 to 4.6 per cent of malignant ovarian neoplasms. One-third occur in women under the age of forty years.[1,8] Since these cells arise from mesenchymal elements, the functional capacity may be unlimited. Granulosa cell tumor is often associated with menstrual irregularities.[9] This patient had minimal menstrual bleeding and elevated urinary estrogens in spite of prior surgical removal of her ovaries.

This patient's clinical picture and many of the other cases of ovarian tumor associated with hypercalcemia[5] have been confused with primary hyperparathyroidism. With hypercalcemia, high normal PTH, hypophosphatemia, and no firm evidence for recurrent ovarian carcinoma, it was felt that hyperparathyroidism was present. The neck exploration disclosed normal-sized parathyroid glands; on light microscopy they were considered normal, and the patient remained hypercalcemic. Only after removal of the recurrent granulosa cell ovarian carcinoma did her serum calcium return to normal.

Summary

Hypercalcemia is uncommonly associated with ovarian carcinoma. When present, it is seen usually with mesonephroma or serous cystadenocarcinoma.

A patient with recurrent ovarian granulosa cell carcinoma and concurrent hypercalcemia was recently treated. A subtotal parathyroidectomy was done, because clinical findings suggested hyperparathyroidism. Normal-appearing glands were found and her serum calcium remained elevated. Later, an abdominal mass became evident and she was re-explored. A recurrent ovarian granulosa cell carcinoma was found and removed, with subsequent return of the serum calcium to normal.

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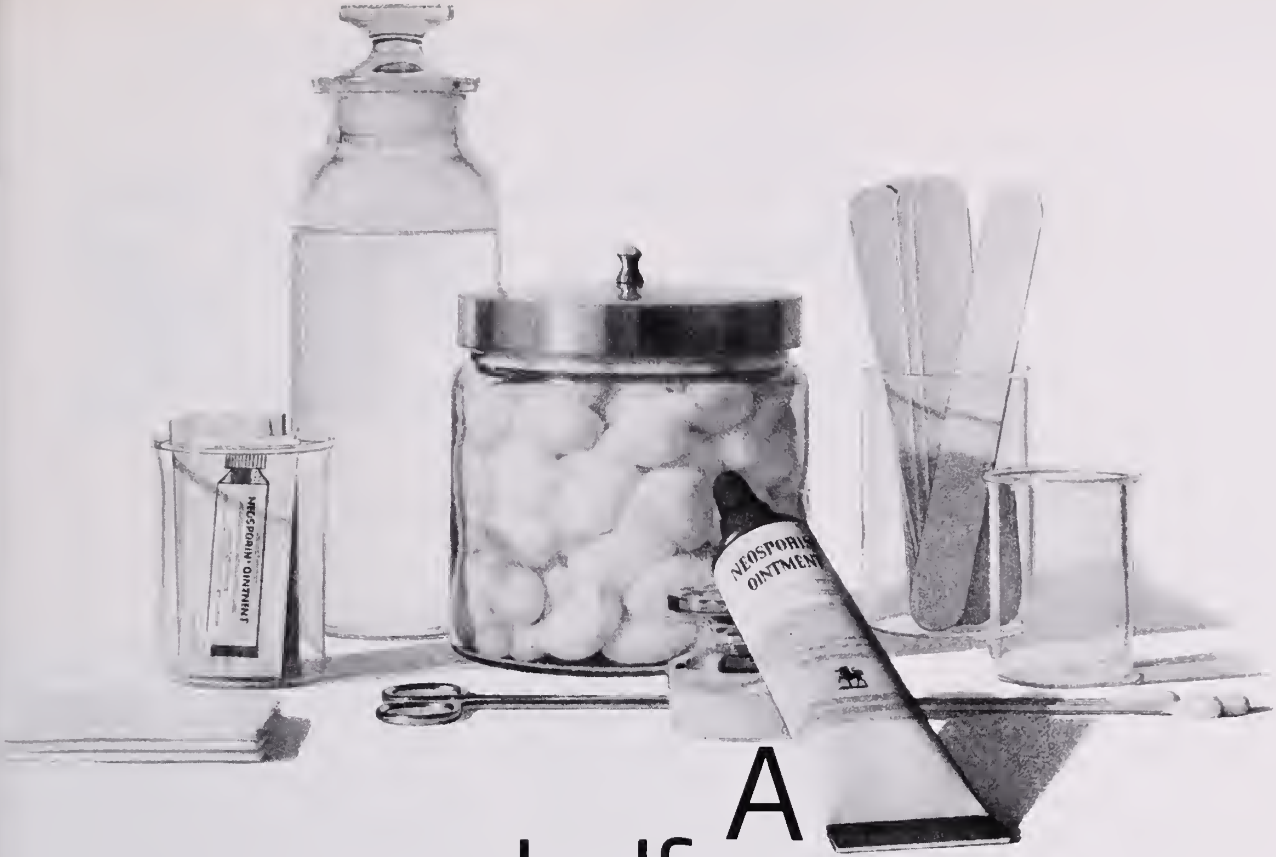

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Nor special K+ rich diets needed as a rule

Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

A medical potpourri

Compiled by Andrew M. Babey, MD, Las Cruces, New Mexico

1. "Life is short, and the plastic period when the brain is apt for acquirement is still shorter. Accordingly, even if all children were fitted for it, it is absolutely impossible to maintain a system of education in which a complete training as a classical scholar is the necessary preliminary to the acquirement of other intellectual disciplines." Whitehead, Alfred North, *The Aims of Education,* Mentor Books, July, 1949, p. 69.

2. "We must remember that the whole problem of intellectual education is controlled by lack of time. If Methuselah was not a well-educated man, it was his fault or that of his teachers. But our task is to deal with five years of secondary school-life. Classics can only be defended on the ground that within that period, and sharing that period with other subjects, it can produce a necessary enrichment of intellectual character more quickly than any alternative discipline director to the same object." *Ibid,* p. 70-71.

3. "There are certain minds, and among them some of the best, for which the analysis of language is not the avenue of approach to the goal of culture. For these a butterfly or a steam-engine has a wider range of significance than a Latin sentence. This is especially the case where there is a touch of genius arising from vivid apprehensions stimulating originality of thought. The assigned verbal sentence almost always says the wrong thing for such people, and confuses them by its trivial irrelevance." *Ibid,* p. 71.

4. "Now the Roman Empire is the bottleneck through which the vintage of the past has passed into modern life. So far as European civilization is concerned the key to history is a comprehension of the mentality of Rome and the work of its Empires." *Ibid,* p. 74.

5. "I simply wish to justify my scepticism as to the claim for Latin literature that it expresses with outstanding perfection the universal element in human life. It cannot laugh, and it can hardly cry." *Ibid,* p. 76.

6. "But the Roman Empire existed by virtue of the grandest application of technology that the world had hitherto seen: its roads, its bridges, its aqueducts, its tunnels, its sewers, its vast building, its organized merchant navies, its military science, its metallurgy, and its agriculture. This was the secret of the extension and the unity of Roman civilization. I have often wondered why Roman engineers did not invent the steam-engine. They might have done it at any time, and then how different would have been history of the world. I ascribe it to the fact that they lived in a warm climate and had not introduced tea and coffee. In the eighteenth century thousands of men sat by fires and watched their kettles boil. We all know of course that Hiero of Alexandria invented some slight anticipation. All that was wanted was that the Roman engineers should have been impressed with the motive force of steam by the humble process of watching their kettles." *Ibid,* p. 80-81.

7. "The marvellous position of Rome in relation to Europe comes from the fact that is has transmitted to us a double inheritance. It received the Hebrew religious thought, and has passed on to Europe its fusion with Greek civilization. Rome itself stands for the impress of organization and unity upon diverse fermenting elements. Roman Law embodies the secret of Roman greatness in its Stoic respect for intimate rights of human nature within an iron framework of empire. Europe is always flying apart because of the diverse explosive character of its inheritance, and coming together because it can never shake off that impress of unity it has received from

Rome. The history of Europe is the history of Rome curbing the Hebrew and the Greek, with their various impulses of religion, and of science, and of art, and of quest for material comfort, and of lust of domination, which are all at daggers drawn with each other. The vision of Rome is the vision of the unity of civilization." *Ibid,* p. 82-83.

8. "Not until long after the fall of the Roman Empire did Western countries adopt the Arabic zero, the sign for the "empty" column of numbers, together with the rudiments of algebra. The zero and Arabic numerals produced a revolution more important than that of the printing press. They liberated mankind from the prison bars of the abacus." Chase, Stuart, *Tyranny of Words,* Harcourt, Brace and Company, 1938, p. 145-146.

9. "To say that philosophers avoid facts is not true. But they are not governed by facts; they are not humble before the facts; facts are not central in their concepts, but come in on tiptoe through the side door." *Ibid,* p. 208.

10. "As an occasional lecturer, I am well aware that it takes resolution, if not courage, to stand up in front of the Middletown Open Forum and say to a questioner from the floor, "I do not know." A kind of shock goes through the audience, as though one had uttered a naughty word. Yet sometimes I have seen that blunt declaration met, after a pause, with a clapping of hands. Perhaps the most important statement in the scientific discipline is "I do not know." *Ibid,* p. 220-221.

11. "Huxley's grandson, Aldous, observes that philosophical arguments are mostly angry shoutings at one another by two people who use the same words but mean different things by them." *Ibid,* p. 241.

12. Speaking of England, Hogben says:

"The machinery of educational selection operates to recruit the nation's statesmen from those who can talk glibly, write elegantly, and argue forcibly, without the capacity to act competently. When the need for action is urgent, they can only continue to talk glibly, write elegantly, and argue forcibly. If democracy can produce only leaders who can talk it is doomed." *Ibid,* p. 336-337.

If A Disability Closed the Door on Your Practice...
Would it also close the door on Your Family's Future?

Disabilities are something a doctor deals with every day. Certainly no one is more aware of how much a life can be affected by a disabling sickness or injury.

Sometimes, though, a doctor can become so involved in the treatment of these disabilities that it becomes easy to put aside thoughts of what might happen to you and your family if that disability struck you down and you were unable to continue your practice.

The Colorado Medical Society has helped to alleviate this problem by making a voluntary program of Disability Income Protection Insurance available to its members.

This plan, which members are able to purchase at Association Group rates, helps see to it that your family will have something to fall back on should you become sick or hurt and unable to work because of a covered sickness or accident.

ACT NOW! Fill out and mail the coupon for details on the Colorado Medical Society's Disability Income Protection Plan. Discover how it can help provide that extra measure of financial security you and your family need. There's no obligation.

MAIL COUPON TO YOUR NEAREST REPRESENTATIVE

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Suite 300
Wheat Ridge, CO 80033

Carl Roderick
2627 West 10th Street
Greeley, CO 80631

Tony Occhiuto
1702 North Circle Drive
P.O. Box 9226, Station A
Colorado Springs, CO 80932

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Colorado Medical Society Insurance Program
Please send me full details on the Disability Income Protection Plan available to me as a member.

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COLORADO

Wood Named President

John M. Wood, MD, Englewood, is an Administrative member of the American Association of Professional Standards Review Organizations, representing the American Association of Foundations for Medical Care, of which Doctor Wood was recently re-elected President for his second term. In addition Doctor Wood serves as Chairman of the Institute for Professional Standards.

Alpert Arthritis Center Dedicated

Dedication of the 22-bed, $1,200,000 Joe and Betty Alpert Arthritis Treatment Center at General Rose Memorial Hospital was held January 30, 1975. Giving emphasis to developing independence in the patient, the Center brings specially trained physicians, nurses, physical therapists, and occupational therapists together to assist the patient in reaching a normal level of function. Mr. Alpert, a major donor, was present. The center memorializes the late Mrs. Alpert. Medical director for the Center is Charley J. Smyth, MD.

Denver Native Named

Dr. Walter Huttner, internist, has been elected president of the Medical and Dental Staff of General Rose Memorial Hospital for 1975-1976. Doctor Huttner, a native of Denver, gained his medical degree at the University of Colorado and completed his internship at Wisconsin General Hospital in Madison, Wisconsin, receiving his postgraduate training at Veterans Hospital in Milwaukee, Wisconsin, and the University of Colorado Medical Center, Denver. He succeeds Dr. Harold J. Hepner, Denver physician, who served as president during 1973 and 1974.

Other new officers of the Rose Hospital Medical and Dental Staff are: Lane D. Craddock, MD, president-elect; Sidney Duman, MD, vice president; and S. Robert Contiguglia, MD, secretary.

Jaffa Plaque Dedicated

A plaque honoring Bertram B. Jaffa, MD, Denver obstetrician who completed his internship and residency at Denver General, and was manager of Health and Charity for Denver from 1928 to 1931, has been dedicated to his memory and placed in the obstetrical delivery area of Denver General's new hospital. After Dr. Jaffa's death in 1949 at the age of 53, the Health and Hospitals structure at W. 7th and Cherokee was named in his honor. This building now is being demolished, and the plaque, which was designed by Denver artist Elizabeth Yanish and is decorated with her design of a tree of life, continues his memory.

MEDICAL SCHOOL NOTES

University of New Mexico Medical Center

Treatments for cancer patients by the 18-million-electron-volt linear accelerator at the University of New Mexico Cancer Research and Treatment Center were initiated in mid-January.

The accelerator, the only one of its kind in New Mexico, is one of the most sophisticated machines of its type, producing high energy x-rays to attack tumors deep within the body.

According to CRTC radiotherapists, the linear accelerator produces high energy x-rays at 10 million volts as well as electrons up to an energy of 18 million volts.

The machine extracts electrons at energy levels up to 18 million volts for treatment of certain superficial tumors managed with difficulty by conventional x-ray machines. The depth of treatment with electrons is controlled by varying the voltage. The higher the voltage, the deeper the treatment.

Electrons permit a relatively uniform distribution of radiation from the surface of the body to a depth determined by the energy. There treatment essentially stops, sparing the underlying normal tissues. This makes it possible to give higher doses to the tumor with decreased side-effects to the patient.

The electron beam can be used in combination with the accelerator's high voltage x-rays, or combined with cobalt treatment, to provide the best distribution of dosage in certain specific areas.

A second unit which is being put into operation is a simulator. This machine defines the area to be irradiated and the direction of the radiation beams. It contains a diagnostic x-ray tube and special imaging system for a better view of the patient's anatomy. The simulator not only improves accuracy, but reduces the time required to plan treatments.

CRTC's linear accelerator, manufactured by the Varian Corporation, is called a Clinac 18. It was purchased at a cost of $320,000 with funding obtained by the Center from the National Cancer Institute and other sources.

University of Nevada
School of Medical Sciences

An HEW grant of $950,063 and a Fleischmann Foundation grant of $375,000 have been made to the University of Nevada, Reno, School of Medical Sciences. Construction of an addition to the Fred M. Anderson Health Sciences Building which will contain a lecture hall, classrooms, research and teaching laboratories is made possible by this grant, which requires a matching of the Fleischmann Foundation grant.

NATIONAL AFFAIRS

Summary of the Actions of House of Delegates American Medical Association 28th Clinical Convention Portland, Oregon November 30-Dec. 4, 1974

A mandatory, special assessment of $60 for AMA members was approved by the House of Delegates at the 28th Clinical Convention in Portland. The assessment, effective Jan. 1, 1975, for AMA members excluding students, interns and residents, is expected to improve immediate cash-flow problems and help build up depleted financial reserves.

Rejecting a $90 dues increase proposed by the Board of Trustees, Delegates instead called for a Special Committee of the House to study the dues issue and report back at the 1975 Annual Meeting.

Meeting for a total of 16 hours and 40 minutes, one third of it devoted to AMA finances and related issues, the House acted on 77 reports and 68 resolutions for a total of 145 items of business.

In addition to taking a positive step to remedy immediate financial problems of the AMA, the House adopted several measures to improve housestaff participation in the Association, heading off a possible defection.

Elections

Bernard J. Pisani, M.D., New York, N.Y., was reelected to a three-year term on the Coordinating Council on Medical Education.

Special Award for Distinguished Service

Ernest B. Howard, M.D., M.P.H., Executive Vice-President on leave from the AMA who will retire March 1, was given a Special Award for Distinguished Service by the House.

Dr. Howard, who joined the AMA in 1948 as Assistant General Manager, was given successive promotions until 1969, when he was named Executive Vice-President. Dr. Howard's prior experience included positions with the Massachusetts Department of Public Health, the Surgeon General's Office of the U.S. Army, and Chief of the Field Party to Peru of the Institute of Inter-American Affairs.

Commendation Resolution

Leo E. Brown, Assistant to the Executive Vice-President of the AMA, was presented with a Commendation Resolution for 24 years of service "to and for American medicine."

Mr. Brown, who will retire early in 1975, joined the AMA in 1950. Serving the House of Delegates at Annual and Clinical Conventions was one of his primary responsibilities.

Report of The President, Malcolm C. Todd

The price of defending medical freedom can be high, but that price must be paid, AMA President Malcolm C. Todd, M.D., told Delegates at the Clinical Convention in Portland.

Equating the freedom that has made American medicine the most creative in the world" with the "very essence of professionalism cherished so highly by the nation's physicians," Dr. Todd pointed out that medicine's freedom, and hence its professionalism, are threatened.

Chief among the threats are various legislative proposals which would impose a compulsory national health insurance system, would make health care a public utility to "reduce each of us to the level of an electric wire or a telephone line," and manpower bills that would "imply indentured service in medical education."

Only a strong AMA can counter such threats and preserve perfessionalism, Dr. Todd emphasized, but "it is impossible for its strength to be any greater than its finances."

Therefore, he issued a strong appeal to the House to support a $90 dues increase, or, as an alternative, a special assessment.

While admitting that the AMA was not 100 per cent effective legislatively, he said that, "No element in society has a perfect score. Any element has to set its sights not on the best of all possible worlds, but the best of all possible realities."

He said that if the AMA is to be effective in seeking a National Health Insurance plan that would "respect both public needs and professional competence," in countering overly-stringent health planning and manpower bills, and in mitigating malpractice problems, then "it will need the money."

Dr. Todd said he personally believed that advertising does "play a useful role in physicians' education on drugs", but that "suspicion is easily planted and spread in these skeptical times, and there is reason to be sensitive to it." He urged careful consideration in the months ahead as to whether advertising should be banned from AMA publications.

In concluding his mid-term address, for which he received a standing ovation, Dr. Todd said:

"I leave you with two questions: Is the survival of our profession in danger? I say that it is. Is a dues increase the necessary price that we must pay for our survival? Again, I say yes. And it seems to me, by God, that no price could be so small for anything so great."

Summary of Actions of The House of Delegates

Because of the wide-ranging nature of the actions taken by the House, and for the sake of clarity, this summary will be divided into five subject areas with appropriate sub-headings as follows:

—Association and Internal Matters of the House
—Physicians and Hospitals and Medical Schools
—Physicians and the Government
—Physicians and the Public
—Miscellaneous

Association and Internal Matters of The House

AMA Finances and Related Matters: In assessing a mandatory, $60 special assessment effective Jan. 1, the Delegates acted to strengthen AMA finances.

The House was reminded that the Association has operated at a defcit for four of the last five years, and that cash reserves have been seriously depleted during that time. In addition, AMA finances in 1974 were adversely affected by inflationary pressures.

After almost six hours of comment and deliberation on Tuesday afternoon and Wednesday morning, the Delegates adopted the $60 special assessment as a stop-gap measure.

The question of a dues increase was referred to a Special Committee of the House to be appointed by the Speaker. The committee will make a comprehensive study of the AMA's financial priorities and capabilities, and report to the House at the 1975 Annual Meeting.

In related actions, the House strongly urged the Board of Trustees to restore in a "holding pattern" the structure of several councils and committees which were to have been eliminated, and to maintain present publication schedules for JAMA, all specialty journals, and Prism.

The House also approved advertising as a legitimate function in AMA publications, and urged that the present full and unrestricted advertising program in AMA publications continue pending further study and a report at the June meeting.

Housestaff Participation in AMA: The Delegates adopted several recommendations designed to strengthen housestaff participation in the AMA.

They include: that the elected Executive Committee of the Intern and Resident Business Session assume advisory responsibilities of the Committee on Housestaff Affairs, which will be dissolved; that programs and priorities of the Department of Housestaff Affairs be developed annually by the department director and the chairman of the I & R Business Session, subject to review and approval of the Board of Trustees; and that responsibility for the editorial content of the Housestaff Newsletter and for the distribution of I & R Business Session reports be exercised by the Session's Executive Committee subject to appropriate approval and review in keeping with Association policies.

In a related action, the House approved an amended resolution calling for the development of model programs to involve medical students in the activities of organized medicine at all levels, and referred it to the Board and the Council on Constitution and Bylaws for implementation.

Professional Liability: During a discussion of malpractice problems, the House adopted a recommendation calling for the Board to give "priority attention" to providing legal counsel and advice to AMA members and state societies in the event their professional liability insurance is not renewed.

The House also emphasized the necessity for state associations to seek legislative remedies for malpractice problems, and directed that the AMA continue to cooperate with the Medical Liability Commission.

Clinical/Scientific Meetings Format Changed: A separation of the fall business meetings of the House and the scientific meetings will be permitted beginning in 1977.

Under bylaws changes adopted by the House in Portland, the House will hold its fall meeting separately in cities recommended by the Board and selected by the House, and the scientific session will hold regional meetings at other times during the year as deemed necessary by the Board and at cities selected by the Board.

The new format was devised to allow regional scientific programming. The scientific assemblies will continue to be held in conjunction with Annual Meetings, however.

In other actions on internal matters, the House:

—Called for a definitive report at the 1975 annual meeting of AMA activities and programs related to PSRO.

—Called for a definitive report at the 1975 annual meeting of AMA activities and programs related to PSRO.

—Rejected a Board of Trustees proposal to replace the Council on Legislation and many functions of the AMPAC Board of Directors with a new Council on Public Affairs.

Referred a report on direct representation in the House of medical specialty societies back to the Council on Consitution and Bylaws for further consideration.

—And adopted a bylaws change permitting past Vice-Presidents of the AMA to become ex-officio members of the House (without voting privileges or reimbursement for meeting expenses).

Physicians and Hospitals and Medical Schools

Due Process: The House adopted several recommendations which reaffirm the rights of all physicians, including housestaff and medical students, to due process. In related actions, the House adopted as AMA policy the proposition that a student's academic records should be open to inspection so that he/she may profit educationally; and referred back to the Judicial Council for further study a report involving three cases of alleged violation of due process at the local level.

Guidelines for Housestaff Contracts: The House adopted a set of revised guidelines for housestaff contracts. The proposed guidelines, as revised, had been approved by the Council on Medical Education, the Board of Trustees, and the Council on Medical Service.

Biomedical Research: The House adopted a 10-point statement on biomedical research urging more federal funding with fewer restrictions. Prepared by the Board, the report sharply criticizes federal cuts in independent research grants and in the budgets of the National Institutes of Health.

The report urges that more unrestricted grants be awarded for research; that NIH be given more independence in establishing budget and research priorities; and that appropriations for biomedical research should be in proportion to other health-related spending.

Continuing Competence of Physicians: Delegates also adopted a Board report calling for strong programs of continuing medical education and peer review as alternatives to relicensure since "the difficulties inherent in relicensure clearly outweigh any potential benefits."

Specific recommendations include all possible encouragement and support for the AMA, constituent societies, JCAH and other bodies in expanding CME programs; that the AMA give high priority to enhancing and reviewing effective methods of continuing competence; that patient satisfaction should be included in performance evaluation; and that well-designed peer review programs be endorsed as an important component of performance evaluation. The House also stressed that evaluation of performance, rather than knowledge per se, is the best method of appraising competence in patient care.

In other actions related to physicians and hospitals and medical schools, the House:

—Adopted an amended resolution which urges that duplication of local peer review procedures be avoided; that medical audit or utilization protocols used in screening be limited to those which are demonstrated to be valid, reliable, and which do not add needlessly to cost; and that when local peer review groups recognize that a hospital medical staff has adequate medical audit and utilization procedures, that fact should be recognized by governmental agencies and JCAH.

—Adopted a Board report detailing legally-approved methods for the exchange of information between and among medical societies and hospitals concerning a physician's hospital privileges or practice.

—And requested that a "comprehensive report" be presented at the 1975 Annual Meeting on questions and issues related to foreign medical graduates.

Physicians and The Government

National Health Insurance: Delegates gave the Board of Trustees a vote of confidence for its efforts to develop new approaches to NHI which maintain traditional AMA goals. The House adopted a Board report containing basic guidelines for NHI deliberations.

The guidelines include minimum federal involvement in the administration of any NHI program; state jurisdiction for licensure of physicians and regulation of insurance; no Social Security tax financing and administration of any program; funding through federal revenues, state revenues, and private funds including employer-employee contributions for private health insurance; comprehensive coverage for basic and catastrophic needs; and the maintenance of pluralism in health delivery.

Manpower and Planning Bills: The House adopted an emergency resolution expressing unanimous opposition to U.S. House of Representatives bills which would divide the nation into health service planning areas and treat health care as a public utility, and which would require medical students to reimburse the government for capitation.

The resolution was unanimously adopted on Wednesday, Dec. 4, and its substance presented to House Speaker Carl Albert and other Congressmen.

Prepaid Plans and Bonuses: Delegates adopted a Judicial Council report which cautions that the payment of bonuses to physicians in prepaid health care plans such as HMO's for minimizing the utilization of services may interfere with the physician's obligations to his patients.

In other actions related to physicians and the government (and third parties), the House:

—Objected to language in insurance letters indicating the claims were "not medically necessary," since this encourages patients to decline to pay for services and is defamatory to physicians.

—Urged that Medicare intermediaries adhere strictly to regulations for reimbursement of chiropractors to those procedures defined in the regulations.

—Encouraged the acceptance and use by physicians of the AMA's Uniform Health Insurance Claim Form, and urged insurors to study the possible use of plastic "charge card" type identification cards for imprinting basic data on insurance forms.

—And urged the government to continue its present 55 m.p.h. speed limit for at least a one-year period, noting that traffic fatalities have declined 14.8% since the speed limit was imposed last year.

Physicians and The Public

Weight Reduction Clinics: The House took a strong policy position against the use of human chorionic gonadotropin for use in weight reduction. The House further resolved "that the AMA warn our citizens about the potential danger of such a weight control program." Clinics utilizing chorionic gonadotropin have been established and widely advertised in various parts of the country.

Child Abuse—The House adopted a substitute resolution encouraging state medical associations to survey child abuse laws in their states, and recommend more desirable legislation where necessary.

Health Care for Disadvantaged—"Vigorous, high-priority" efforts to foster health care programs for disadvantaged segments of the population were recommended to the Delegates.

The reference committee report noted that the Council on Medical Service will continue to develop and implement long-range strategies to improve health care of the poor. The House requested regular reports of progress made.

Maternity and Newborn Care—The House adopted two reports which reaffirm AMA policy to encourage insurance coverage of the newborn from the moment of birth, urge the health insurance industry to offer coverage for obstetrical care and any complications, and recommend that the insurance industry—as well as government—offer such coverage on the broadest possible basis.

Miscellaneous Actions of The House

In other actions relative to physicians and the public, the House:

—Supported state legislation to regulate the practice of acupuncture. The new policy says acupuncture should only be performed in research settings by a physician or under the direct supervision of a physician. . . .

—Reaffirmed AMA endorsement of the fluoridation of water supplies. . . .

—Adopted a Judicial Council report which holds that, "It is not unethical for a physician to authorize the listing of his name and practice in a (community) directory for professional or lay use which is intended to list all physicians in the community on a uniform and nondiscriminatory basis. The listing shall not include any self-aggrandizing statement or qualitative judgment regarding the physician's skills or competence." . . .

—Endorsed the right of a physician to dispense ampicillin-probenecid for gonorrhea patients, reflecting a Judicial Council opinion that physicians have a duty to protect the confidentiality of patients who contract gonorrhea. . . .

—And adopted a substitute resolution calling for the government to develop adequate safeguards for the transportation and storage of hazardous materials such as radioactive materials. . . .

John M. Wood, M.D.
Robert E. McCurdy, M.D.
Kenneth A. Platt, M.D.

Perinatal Care Grant

A regional continuing education program on the care of high-risk newborns which has resulted in the improvement of care for babies and their mothers has received continued funding from the National Foundation/March of Dimes in the amount of $47,525 for 1975.

The Medical Service Grant has been made to The Children's Hospital in Denver for the Perinatal Care Educational Project which the Hospital conducts in cooperation with the University of Colorado Medical Center.

L. Joseph Butterfield, MD, director of the Children's Department of Neonatology, and Fred Battaglia, MD, professor and chairman, Department of Pediatrics, UCMC, said that in 1974 the project used three methods to reach out to medical personnel and hospitals in the seven-state region served by Denver's cooperative newborn intensive care service:

1. Perinatal Care Educational Workshops in 16 cities in Colorado, Kansas, Wyoming, Nebraska and Montana.
2. Site visits at 28 hospitals.
3. Traineeships provided three ways for medical personnel to gain new information:
    - a. Unit visits — tutorial supervision for the Newborn Centers at Children's and UCMC.
    - b. Evening courses — High-risk newborn classes (22 hours) in Denver and outlying areas.
    - c. Weekly fellow-residents visits.

The goals of the continuing education program are to upgrade the skills of medical personnel to provide the best care possible for babies, even in the smallest hospitals, and to foster a regional network for moving high-risk infants to intensive care centers, said Dr. Butterfield.

in Brief

A summary of AMA, medical & health news

American Medical Association / 535 North Dearborn Street
Chicago, Illinois 60610 / Phone (312) 751-6000 / TWX 910-221-0300

Membership incentives programs will again be offered to state and county medical societies by the AMA in 1975. The programs, which were successful in 1974, encourage early AMA dues transmittal and membership recruitment. The state incentives program pays constituent societies ½% interest above current 180-days treasury bill rates on the day AMA dues are received at AMA Headquarters and from that day to April 30. The 1975 program began Jan. 1. The county incentives program pays county societies half the year's dues for new housestaff and medical student members and half of the year's dues for regular members who resume membership after being out of the AMA for 24 consecutive months or more.

Further development of a federation that is "structurally resilient, financially independent, scientifically respected, and supported by a participating membership," is the basic priority of the AMA for 1975. A statement of current AMA priorities, submitted by the Board of Trustees, was adopted by the House of Delegates in December. The priorities will be one element in the 1975 planning cycle of the AMA's long range planning program. To accomplish priorities, the statement called for closer ties with medical societies; greater involvement by individual members at all levels of the federation; and a "financially self-reliant central organization."

Bylaws amendments approved by the AMA House of Delegates will provide for partial separation of House and scientific meetings, effective in 1977. Clinical Conventions will be held in Honolulu in 1975 and in Philadelphia in 1976. After that the House will hold an interim meeting each fall, possibly in Chicago, and the Council on Scientific Assembly will sponsor several regional postgraduate courses at various cities throughout the year. The Scientific Assembly still will meet in conjunction with the House at each Annual Convention.

"The Medical Aspects of Sports-15" has been published by the AMA with the support of the Sports Medicine Foundation of America. The book includes articles on research, nutrition, drugs, female athletics, head and neck injuries, basketball and tennis, and rehabilitation following surgery. It is designed for practicing physicians and students. OP-423 is available for $1 from Order Dept., AMA Headquarters.

MEETINGS

**University of Utah College of Medicine,
Department of Anesthesiology**

20TH ANNUAL ANESTHESIOLOGY COURSE

**C'est Bon Hotel Convention Center,
Park City, Utah**

February 14-18, 1975

Contact: Department of Anesthesiology, University of Utah Medical Center, 50 North Medical Drive, Salt Lake City, Utah 84132.

**American Lung Association of Colorado—
American College of Chest Physicians**

14TH ANNUAL JOHN R. DURRANCE MID-WINTER CHEST CONFERENCE

Given Institute of Pathobiology, Aspen, Colorado

February 22-25, 1975

Contact: John A. Sbarbaro, MD, Colorado Trudeau Society, 1600 Race Street, Denver, Colorado 80206.

**Colorado Association for
Continuing Medical Laboratory Education**

PARASITOLOGY

CACMLE Center, Mercy School of Nursing Building, 16th at Milwaukee St., Denver.

February 24-26, 1975

Contact: CACMLE, Inc., Box 84, Mercy School of Nursing Building, 1601 Milwaukee St., Denver, Colorado 80206.

**Penrose Hospital—
Society of Nuclear Medicine**

FOURTH ANNUAL THYROID SYMPOSIUM

Vail Hilton Inn, Vail, Colorado

February 24-28, 1975

Contact: Thomas A. Verdon, Jr., Chief, Nuclear Medicine Service, Veterans Administration Hospital, Columbia, Mo.

International Medical Assembly

39TH ANNUAL INTERNATIONAL MEDICAL ASSEMBLY

St. Anthony Hotel, University of Texas Medical School, San Antonio, Texas

February 27-28, 1975

Contact: Mr. S. E. Cockrell, Jr., 202 West French Place, San Antonio, Texas 78212.

Colorado Medical Society

WINTER CLINICS

Swedish Medical Center Complex, 501 East Hampden Avenue, Englewood, Colorado.

February 28-March 2, 1975

Contact: Mrs. Shirlee Myers, Colorado Medical Society, 1601 East 19th Avenue, Denver, Colorado 80218.

Mount Airy Psychiatric Center

FIFTH ANNUAL MOUNT AIRY FOUNDATION GOLD MEDAL SEMINAR, LUNCHEON AND BANQUET

Brown Palace West Ballroom, Denver, Colorado

March 1, 1975

Contact: Mount Airy Psychiatric Center, (303) 322-1803.

Beth Israel Hospital Foundation

ASPEN RADIOLOGY CONFERENCE

**Aspen Institute for Humanistic Studies,
Aspen, Colorado**

March 3-7, 1975

Contact: Maurice O'Connor, MD, Conference Director, Division of Radiology, Denver General Hospital, Denver, Colorado 80204.

this way to Skiing

Society for Behavioral Kinesiology, Inc.

SECOND ANNUAL CONFERENCE

Capitol Plaza Inn, Denver, Colorado

March 5-7, 1975

Contact: Elizabeth Littell, Society for Behavioral Kinesiology, Inc., 5423 Grape Street, Houston, Texas 77035.

American College of Physicians

UTAH REGIONAL MEETING

Friare Travelodge, Salt Lake City, Utah

March 7, 1975

Contact: Donald E. Smith, MD, 2914 Millicent Drive, Salt Lake City, Utah 84108.

PURGATORY SKI SYMPOSIUM

North of Durango, Colorado

March 7-8, 1975 ☜

Contact: David R. Holten, MD, 8517 Osuna Rd., NR, Albuquerque, New Mexico 87109.

The Children's Hospital

COLORADO CONFERENCE ON PEDIATRIC NEPHROLOGY

Given Institute of Pathobiology, Aspen, Colorado

March 10-12, 1975 ☜

Contact: Larry G. McLain, MD, Division of Nephrology, The Children's Hospital, Denver, Colorado 80218.

University of Utah College of Medicine

3RD ANNUAL SYMPOSIUM ON SURGERY OF THE HAND

Snow Bird Resort, Snow Bird, Utah

March 12-14, 1975 ☜

Contact: Earl Z. Browne, Jr., MD, Division of Plastic Surgery, University Medical Center, 50 North Medical Drive, Salt Lake City, Utah 84132.

American Medical Association—
American Bar Association

1975 NATIONAL MEDICOLEGAL SYMPOSIUM

MGM Grand Hotel, Las Vegas, Nevada

March 14-16, 1975

Contact: MGM Grand Hotel, Convention Reservations, P.O. Box 11087, Las Vegas, Nevada 89111.

American Urological Association, Allied

BI-ANNUAL SEMINAR

Craig Rehabilitation Hospital Conference Room, 3425 S. Clarkson St., Englewood, Colorado.

March 15, 1975

Contact: Donna Hoffman, Colorado Urological Center, PC, 1245 E. Colfax Avenue, Denver, Colorado 80218.

Announcement:

The Rocky Mountain Region Kidney Foundation has recently awarded a fund to help pay for hearing aids needed by kidney patients with hearing loss. This region covers a four-state area including Colorado, Wyoming, Montana and Idaho. Patients with chronic renal disease, who reside in this area, are eligible for this assistance.

The Regional Foundation has shown an active interest in rehabilitation needs of individuals with chronic renal disease; it is an affiliate of the National Kidney Foundation, the only national voluntary health agency directed toward the prevention, treatment and cure of kidney disease.

Publication rules and suggestions to authors

1. Who may submit articles. The Rocky Mountain Medical Journal ordinarily accepts only articles prepared by members of the state societies we serve and by guest speakers at their official meetings.

2. Method of preparation. All material for publication must be typewritten, double spaced, with liberal margins, using only one side of the paper, pages consecutively numbered, and preferably on standard 8½ x 11 white bond paper. Carbon copies are *not* acceptable.

Title (preferably short) and author's name, city and state must appear at the top of the first page. Second and subsequent pages should be identified with consecutive page numbers and author's surname. If physician authors possess more than one degree, the MD only is used. Lesser degrees of non-MD authors or co-authors may be used.

Please include beneath the title or at the top of the first page a brief paragraph stating what the article is designed to show and, therefore, why it should be read. This introductory feature is, in editorial parlance, called the "blurb"; it is printed in bold type.

3. Where to submit material. All copy must be sent to the editor for the state in which the material originates. Editors for each state, with their mailing addresses, are listed monthly on the Table of Contents page of the Journal.

4. Acceptance or rejection. The state editor will (1) tentatively accept the article, (2) return it to the author with suggestions for revision, or (3) reject it. He will edit and forward approved copy to the publication office in Denver for final editing and scheduling.

5. Order of publication. Ordinarily, articles will be published in the order received. Those whose value is seasonal, whose value would be lost if publication is delayed, or which reflect priority of original research, are given special consideration. State presidential addresses, programs, state society minutes, and timely organization announcements are given priority.

6. Length of articles. Scientific papers should be "boiled down" not to exceed ten pages of double-spaced typewritten standard 8½ x 11 inch sheets. Shorter papers are more acceptable to editors and readers, and earlier publication is probable. Every journal is in competition for the reader's time, and condensation is the order of the day. For this reason, and because of financial and space limitations, we request that copy be condensed to the greatest extent consistent with conveying the message.

7. Illustrations. A limited number of illustrations or "cuts," usually up to six, will ordinarily be accepted within our own publication budget if the editor believes they enhance the value of the article. Clear photos, simple diagrams or line drawings in black on white, printing rather than writing, reproduce well. Cuts should be mounted separately, and the paper or cardboard mounts should be the same size as that upon which the article is typed. Each should have its caption below: Fig. 1, Fig. 2, etc., with a short descriptive sentence. Authors will be billed our cost for excess above six cuts.

8. Tables. Tables should be simple, presenting only brief relevant data, amply spaced. They should be placed at the back of the manuscript on separate sheets. Each should have its number and title above: Table 1, Title; Table 2, Title; etc. Long, large, or complicated tables ordinarily are not acceptable.

9. Case reports. Case reports are popular with our readers. A brief introductory statement concerning the condition or disease, tells why the case is presented. The report follows with a separate heading, CASE REPORT or CASE 1, CASE 2, etc. Include only relevant, positive laboratory and other data. Names, initials, and numbers are unimportant; age, sex, and sometimes occupation are significant. Minimize dates; then make it month, date, year—as February 9, 1969; not 2/9/69. After the case presentation, review or sum it up under a heading such as Discussion, Comment, Summary or Conclusion.

10. Footnotes. Footnotes must be brief. One at the bottom of the first page should state the Society and date of presentation, and institutional origin, if any. Special titles or position of the author, acknowledgements, etc., will be added according to simplicity, editorial policy and discretion.

11. References. Reference lists rarely add to the value of an article for the majority of readers. We will make every effort to publish short reference lists, but long ones will be deleted. Incidentally, the proper heading is "References," not "Bibliography." The latter implies everything in the literature upon the subject. Make them uniform in style and brief, as: Jones, W. K.: Pyelonephritis in Infancy. JAMA 141:75. 1964.

12. Editorials. We would like to have more submitted by our State editors and the membership at large. Readers must get tired of thunder from publication headquarters in Denver; frankly, we do too! Speak out, and we'll sign your name, initials, or respect your request for anonymity, as you choose. If you don't like something we do or say, please let us in on it; we could even stand to hear about it if something happens to please you. A "Letter to the Editor" may help you get something off your mind. We're asking for it and we have a place to put it—in the Journal, that is!

13. Proofs. Galley proofs are submitted to the author, and prompt return is essential. Authors should correct typographical, grammatical, or rhetorical errors, but do not reinsert or rewrite sentences, paragraphs, tables, etc., which an editor may have deleted, condensed, or paraphrased. When an article reaches the galley-proof stage, the author may NOT re-edit his article; that is the privilege of the Journal's editors.

14. Reprints. Most authors desire reprints. Our printing firm provides them on a non-profit basis. They MUST be ordered when the author submits his corrected proof.

15. Our Journal is copyrighted. We and most state and regional journals owned by state medical societies have granted each other continuing copyright permission to copy or quote with proper credit. Copyright permission is not granted to commercial or privately owned publications.

OBITUARIES

Colorado

Walter A. Ohmart, MD, died at his home, 631 Monroe St., Denver, June 11, 1974 after a long illness. He was 85 years of age. Born May 30, 1889 in North Manchester, Indiana, he was educated in the public schools of that community. He received his MD from the University of Indiana in 1917, and after a year of internship at the Indianapolis City Hospital he joined the armed forces to serve in World War I. Following the war he moved to Colorado and set up an office for general practice in Pueblo. In 1920 he moved his practice to Denver, and in 1930 enrolled at the University of Colorado for graduate training in ophthalmology. Receiving his degree as Doctor of Ophthalmology in 1932, he opened a practice in Denver. He was certified by the American Board of Ophthalmology in 1934. He remained on the faculty of the University of Colorado for 25 years, achieving the academic rank of Assistant Clinical Professor of Ophthalmology.

Doctor Ohmart was a member of the Denver county and Colorado medical societies and the American Medical Association. He was a past president of the Colorado Ophthalmological Society and a member of the American Academy of Ophthalmology and Otolaryngology. He belonged to the Phi Rho Sigma medical fraternity and the Sigma Xi scientific fraternity. He was a Shriner and a Kiwanian. He was on the consulting staffs of Children's, Presbyterian, and St. Anthony's hospitals, and was a member of the Active Staff of Denver General Hospital, having served as Staff Vice-President one year. He was awarded the Selective Service Medal for his services at Lowry Air Force Base and Fitzsimons Army General Hospital during World War II.

Doctor Ohmart was married to Marie T. Dixon in Indianapolis, December 28, 1918. Mrs. Ohmart survives the doctor as does a son Walter A. Ohmart, Jr., Denver. Also surviving are a brother, Dr. Galen B. Ohmart of Sarnia, Ontario, Canada; two sisters, Mrs. Ruth Carlin, Warsaw, Indiana, and Mrs. Mary Carrol, Chillicothe, Ohio, and four grandchildren.

* * * *

Howard H. Heuston, MD, Boulder, died Friday afternoon, January 3, 1975 in the Boulder Community Hospital. He suffered a severe heart attack about noon of the day he died. He was born May 1, 1886 in Glenvil, Nebraska of pioneer parents. In his early boyhood the family moved to Oklahoma then known as the Indian Territory. After acquiring a BA from Valparaiso University in Indiana he taught school in Nebraska, Oklahoma, and Oregon.

At the age of 29 years he decided to become a physician and enrolled in the University of Colorado School of Medicine then situated in Boulder. After his first two years he transferred to Washington University, St. Louis, Mo., from which he received his MD in 1919. After an internship in St. Louis City Hospital he returned to Boulder and became associated in the practice of medicine with the late Dr. Carbon Gillaspie.

Doctor Heuston was a member of the Boulder County Medical Society (President, 1924), the Colorado Medical Society, and the American Medical Association. He was a Fellow in the American College of Surgeons. He was a Rotarian and belonged to the Methodist Church.

In 1921 he was a leader in the Boulder Hospital Association, acquired property, and later constructed what is now the Boulder Community Hospital. He was at one time Chief of Staff of that institution. In 1949 he founded what is now the Boulder Medical Center.

In addition to his activities in medical circles he was interested in civic affairs. He was elected to the Boulder City Council in 1928, and was elected Mayor in 1932, an office he held until 1940 when he chose not to run. During his tenure in office he laid the groundwork for the city's future growth. He planned many civic improvements, most of which have materialized over the years. He was very active in the Boulder Chamber of Commerce.

On January 12, 1921 he was married to Louise T. Curtis, a nurse he met while attending medical school. Mrs. Heuston survives as do a daughter, Mrs. Helen Harper of Medford, Oregon; three sons, William C., Bloomfield Hills, Michigan; Robert H., Evanston, Illinois; and Phillip T., Marion, Mass. Seven grandchildren and four great-grandchildren also survive.

* * * *

Willis B. Hardesty, MD, Berthoud, Colorado, died December 1, 1974 after a brief illness. Born May 5, 1883 in Winfield, Missouri, he received his MD from the University of Colorado in 1916, and was licensed to practice medicine in Colorado July 5 of that same year. He opened an office for general practice in Berthoud in that year, and continued in the same location until shortly before his death.

He was a member of the Larimer County and Colorado medical societies, and of the American Medical Association. He was a Mason and an Elk and a member of the Berthoud Chamber of Commerce. He was on the active staff of the Longmont United Hospital and was an honorary member-emeritus of Loveland Memorial Hospital.

Doctor Hardesty was married to Lena Clara Hutcherson in Denver, December 25, 1912. Mrs. Hardesty died October 9, 1965. Surviving the doctor are a son, John F. Hardesty, Los Angeles, California, and a daughter, Mrs. Marian Bayers, St. Louis, Missouri, five grandchildren, and four great-grandchildren.

Leon Block, MD, Denver, died May 31, 1974. Born 82 years ago in Waco, Texas, he spent his earlier years in Pueblo, Colorado. He received his MD from the University of Colorado in 1912, then specialized in diseases of the eye, ear, nose, and throat. He pioneered in cataract surgery and corneal transplants.

He was a Captain in the Army Medical Corps during World War I, receiving the Congressional Medal of Honor and the Silver Star.

Doctor Block was a member of the Denver County and Colorado medical societies and of the American Medical Association. He received his 50-year award from the Colorado Medical Society in 1962. He had served on the staffs of General Rose, Presbyterian, Beth Israel, and Colorado General hospitals.

His wife of 51 years, Bertha May, survives him, as do a daughter, Mrs. Herbert Berger, a sister, Dora Alexander, Woodland Hills, California; a brother, Dr. Harry Block, Oakland, California, three grandchildren, and one great-grandchild.

* * * *

Stanley W. Strunk, MD, died Monday, January 6, 1975 at St. Joseph Hospital in Denver. He was 40 years of age. Born December 3, 1934 in Decorah, Iowa, he received his undergraduate education as well as his MD from the University of Washington, Seattle. He was an honor student throughout his educational career.

Following graduation he joined the faculty of the University of Washington, then later became a member of the staff of the Armed Forces Institute of Pathology in Washington, D.C. Following this, he joined the academic ranks at Southwestern University Medical School, Dallas, Texas, in which city he became pathologist to the Veterans Administration Hospital. In 1963 he became pathologist at St. Joseph Hospital, Denver, and held the academic rank of Clinical Assistant Professor of Pathology at the University of Colorado School of Medicine.

Doctor Strunk was a member of the Denver county and Colorado medical societies and of the American Medical Association. He belonged to the College of American Pathologists, the Colorado Society of Clinical Pathologists, the International Academy of Pathology, and the American Society of Cytology.

On August 22, 1953 he married Janet A. Webber who survives him. Also surviving are three sons, Richard J., Lakewood; Stephen R. of Greeley, and Michael W., currently attending Colorado State University, and a daughter, Miss Linda M., Lakewood. His parents, Dr. and Mrs. William R. Strunk, Ventura, California, also survive.

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SOCIETY OFFICERS

Colorado Medical Society

OFFICERS—1974-75—terms of Officers and Committeemen expire at the Annual Session of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: Howard T. Robertson, Denver.

President-elect: Joseph S. Pollard, Jr., Colorado Springs.

Vice President: Harlan B. Huskey, Fruita.

Treasurer: Otis J. King, Jr., Colorado Springs.

Constitutional Secretary: Stanley J. Sontag, Lakewood.

Delegates to the A.M.A.: John M. Wood, Englewood, Dec. 31, 1975; Robert E. McCurdy, Denver, Dec. 31, 1975; Kenneth A. Platt, Westminster, Jan. 1, 1975-Dec. 31, 1976.

Alternate Delegates to the A.M.A.: Kenneth A. Platt, Westminster, Dec. 31, 1974; Clyde E. Stanfield, Denver, Dec. 31, 1976; William Y. Takahashi, Boulder, Dec. 31, 1975; Joseph L. Kovarik, Dec. 31, 1975. One position to be filled.

Speaker, House of Delegates: Robert A. O'Dell, Aurora.

Vice Speaker, House of Delegates: R. Jack Warren, Denver.

Foundation Advocate: H. Sol Cersonsky, Denver.

Scientific Editor for Colorado and Chairman of the Editorial Board, Rocky Mountain Medical Journal: Carl H. McLauthlin, Denver.

Scientific Editor Emeritus, Rocky Mountain Medical Journal: Douglas Macomber, Denver.

Executive Director: Mr. Donald G. Derry, 1601 East 19th Avenue, Denver, Colorado 80218. Telephone (303) 534-8580.

New Mexico Medical Society

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Session in the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: U. G. Hodgin, Jr., Albuquerque.

President-elect: Robert Cutler, Espanola.

Vice President: Walter Hopkins, Lovington.

Secretary-Treasurer: Ronald V. Dorn, Jr., Albuquerque.

Immediate Past President: Armin T. Keil, Raton.

Speaker, House of Delegates: William J. Hossley, Deming.

Vice Speaker, House of Delegates: John D. Abrums, Albuquerque.

Delegate to A.M.A.: Emmit M. Jennings, Roswell.

Alternate Delegate to A.M.A.: Armin T. Keil, Raton.

Councilors for Three Years: George P. Bunch, Las Vegas; Robert Zone, Santa Fe; Livingston Parsons, Albuquerque; John Moore, Roswell.

Councilors for Two Years: James Loucks, Los Alamos; William C. Gorman, Albuquerque; Donald Wolfel, Albuquerque; James Gaba, Artesia; Jerome P. Pucelik, Las Cruces; Theodore Draelos, Silver City; Donald Draney, Alamogordo.

Councilors for One Year: Edgar Smith, Albuquerque; John G. Griffin, Albuquerque; Samuel Neff, Clovis; T. G. McCormick, Hobbs; Norton Ritter, Gallup; Jack Coats, Farmington.

Scientific Editor for New Mexico Rocky Mountain Medical Journal: Marcus J. Smith, Santa Fe.

Assistant Scientific Editor for New Mexico, Rocky Mountain Medical Journal: William S. Curran, Albuquerque.

Associate Editor for New Mexico, Rocky Mountain Medical Journal: Mr. Ralph R. Marshall, Albuquerque.

Executive Director: Mr. Ralph R. Marshall, 3010 Monte Vista Blvd., NE, Albuquerque, 87106. Telephone (505) 265-8494.

Associate Executive Director: Rick Beitler, Albuquerque.

Montana Medical Association

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Meeting of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Meeting.

President: John R. Halseth, Great Falls.

President-elect: David Gregory, Glasgow.

Vice President: Colvin H. Agnew, Billings.

Secretary-Treasurer: Robert P. Yost, Missoula.

Assistant-Secretary-Treasurer: James E. Elliott, Havre.

Delegate to the A.M.A.: Herbert T. Caraway, Billings.

Alternate Delegate to the A.M.A.: Mark B. Listerud, Wolf Point.

Executive Committee: John R. Halseth, Great Falls; David Gregory, Glasgow; Colvin H. Agnew, Billings; Robert P. Yost, Missoula; James E. Elliott, Havre; Herbert T. Caraway, Billings; Mark B. Listerud, Wolf Point; John R. Burgess, Jr., Helena; James K. Cope, Forsyth.

Scientific Editor for Montana, Rocky Mountain Medical Journal: Gerald A. Diettert, Missoula.

Associate Editor, Rocky Mountain Medical Journal: Mr. G. Brian Zins, Helena.

Executive Director: Mr. G. Brian Zins, 2021 11th Avenue, Suite 12, Helena, Montana 59601, Teelphone (406) 443-4000.

Nevada State Medical Association

OFFICERS—Terms of Officers and Committeemen expire in April 1976.

President: William K. Stephan, Las Vegas.

President-elect: John W. Callister, Reno.

Secretary-Treasurer: John L. Holmes, Las Vegas.

Immediate Past President: Thomas K. Hood, Elko.

Delegate to A.M.A.: Norman Christensen, East Ely.

Alternate Delegate to A.M.A.: Richard C. Inskip, Reno.

Scientific Editor for Nevada, Rocky Mountain Medical Journal: Thomas J. Scully, Reno.

Assistant Scientific Editor for Nevada, Rocky Mountain Medical Journal: Robert W. Williams, Las Vegas.

Associate Editor, Rocky Mountain Medical Journal: Mr. Richard G. Pugh, Reno.

Executive Director: Mr. Richard G. Pugh, 3660 Baker Lane, Reno 89502. Telephone (702) 825-6788.

Wyoming State Medical Society

OFFICERS—1975—Terms of Officers and Committeemen expire December 31, 1975. Terms of office (with the exception of Delegate and Alternate Delegate to A.M.A.) expire at the end of the calendar year rather than at the Annual Session.

President: Donald B. Hunton, Cheyenne.

President-elect: Patrick D. Nolan, Buffalo.

Vice President: James E. Stoetzel, Pine Bluffs.

Secretary: Kent T. Christensen, Casper.

Treasurer: James R. Alexander, Torrington.

Delegate to A.M.A.: Fenworth M. Downing, Sheridan.

Alternate Delegate to A.M.A.: John J. Corbett, Casper.

Speaker of the House: Theodore L. Johnston, Cheyenne.

Vice Speaker of the House: Ross J. Collie, Lander.

Immediate Past President: Paul R. Yedinak, Rock Springs.

Scientific Editor for Wyoming, Rocky Mountain Medical Journal: Francis A. Barrett, Cheyenne.

Associate Editor for Wyoming, Rocky Mountain Medical Journal: Mr. Robert Smith, Cheyenne.

Executive Director: Mr. Robert Smith, P. O. Drawer 4009, Cheyenne, Wyoming 82001. Telephone (307) 635-2424.

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In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).
Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.
ADVERSE REACTIONS: **Gastrointestinal** (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region
Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).
Renal toxicity: rise in BUN apparently dose related (See **WARNINGS**)
Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus
Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.
Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.
Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands, no abnormalities of thyroid function studies are known to occur.
USUAL DOSAGE: **Adults**—600 mg daily, divided into two or four equally spaced doses. More severe infections an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule 900 mg initially, followed by 300 mg q i.d for a total of 5 4 grams
For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended
Eaton Agent pneumonia 900 mg daily for six days.
Children—3 to 6 mg/lb/day divided into two to four equally spaced doses
Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided
Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated Food and some dairy products also interfere Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.
In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.
In streptococcal infections, a therapeutic dose should be given for at least 10 days.
SUPPLIED: Rondomycin' (methacycline HCl): 150 mg and 300 mg capsules, syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73

WALLACE LABORATORIES
CRANBURY, NEW JERSEY 08512

When the focus is on bronchitis due to susceptible strains of *H. influenzae* and pneumococci*

Rondomycin® 300 mg.
Capsules
[methacycline HCl]

Delivers from the very first dose:

tudies show that after the first dose serum levels rapidly rise above minimum *in vitro* inhibitory concentrations

*Since many strains are known to be resistant, routine sensitivity testing is recommended.

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Rocky Mountain Medical Journal

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March 1975

VOLUME 72 • NUMBER 3

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GE OF PHYSICIANS
PHILADELPHIA
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MDS

Both often

Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequen
and/or severity of grand mal seizures m
require increased dosage of standard an
convulsant medication; abrupt withdraw
may be associated with temporary increase in frequency and/or severity of
seizures. Advise against simultaneous in
gestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to
those with barbiturates and alcohol) hav
occurred following abrupt discontinuanc
(convulsions, tremor, abdominal and mu
cle cramps, vomiting and sweating). Kee
addiction-prone individuals under carefu

respond to one

According to her major
mptoms, she is a psychoneu-
tic patient with severe
xiety. But according to the
scription she gives of her
elings, part of the problem
ay sound like depression.
his is because her problem,
though primarily one of ex-
ssive anxiety, is often accom-
anied by depressive symptom-
ology. Valium (diazepam)
n provide relief for both—as
e excessive anxiety is re-
eved, the depressive symp-
ms associated with it are also
ten relieved.

There are other advan-
ges in using Valium for the
anagement of psychoneu-
tic anxiety with secondary
epressive symptoms: the
sychotherapeutic effect of
alium is pronounced and
pid. This means that im-
rovement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium®
(diazepam)
2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

urveillance because of their predisposi-
on to habituation and dependence. In
regnancy, lactation or women of child-
earing age, weigh potential benefit
gainst possible hazard.

recautions: If combined with other psy-
hotropics or anticonvulsants, consider
arefully pharmacology of agents em-
loyed; drugs such as phenothiazines,
arcotics, barbiturates, MAO inhibitors
nd other antidepressants may potentiate
s action. Usual precautions indicated in
atients severely depressed, or with latent
lepression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

ROCHE
Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

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OUR COVER

Animas Forks in the Colorado wilds, near Lake City, up from Ouray, once contained a number of ostentatious dwellings like this, left over from a surge of mining activity in the late 1870s when it was "the largest city at 11,300 feet." More than 1,000 people settled in to probe its mines. Thomas Walsh, and perhaps his daughter Evelyn, lived and worked there, adding to the fortune which ultimately brought the Hope diamond to her jewel box. Otto Mears built a railroad spur up from Eureka, but even Eureka, along with Animas Forks, is no longer a place on the map. Credit: Michael S. Kappy, MD, Commerce City, Colorado.

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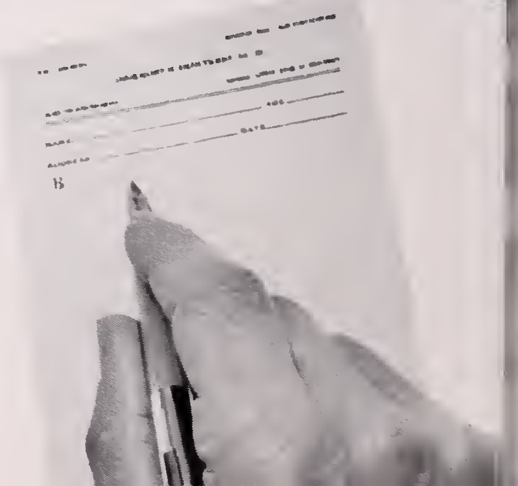
Bioequivalence



he weight of scientific opinion:

If the pharmacist substituted a
emically equivalent drug for the
e you have specified for your
tient—could you be certain of that
oduct's safety and effectiveness
nply because the chemical content
as the same?

Definitely not, unless bio-
uivalence tests and other quality
surance checks had been conducted.
he pharmaceutical industry and
any scientists have maintained this
sition for years, but others have
estioned it. Now the Office of
chnology Assessment of the
ongress of the United States has
ported on the issue in its Drug
ioequivalence Study.*

Here are a few definitive state-
ents in the O.T.A. report:
"...the problem of bioinequiva-
ncy in chemically equivalent prod-
cts is a real one. Since the studies in
hich lack of bioequivalence was
emonstrated involved marketed
roducts that met current compen-
ial standards, these documented in-
tances constitute unequivocal
vidence that neither the present
tandards for testing the finished
roduct nor the specifications for
aterials, manufacturing process,
nd controls are adequate to ensure that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.

DRUG
BIOEQUIVALENCE

A REPORT OF THE
OFFICE OF TECHNOLOGY ASSESSMENT
DRUG BIOEQUIVALENCE STUDY PANEL

"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and
(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or
(c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...

P·M·A

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the
ntegrity of
your prescription

When low back pain* interferes...

Help relieve pain, restore mobility with

PARAFON FORTE® Tablets

chlorzoxazone † 250 mg.; acetaminophen 300 mg.

*This drug has been evaluated as "probably" effective for this indication.

See brief summary of prescribing information on facing page for Indications, Contraindications, Warnings, Precautions and Adverse Reactions.

©McN 74

PARAFON FORTE® tablets help relieve pain, restore mobility and stop pain-spasm feedback by providing:

a nonsalicylate analgesic equal to aspirin for relief of pain,[1,2] yet unlikely to cause the gastric irritation,[2,3] allergic reactions[2] or increased bleeding time[4] associated with aspirin therapy...

and a skeletal muscle relaxant shown in extensive clinical studies to afford relief of discomfort in acute musculoskeletal conditions*[5-7] but which is not an antihistamine or tranquilizer derivative and is unlikely to produce a tranquilizing or sedative effect.[5,7,8]

* **Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.
Warnings: *Usage in Pregnancy*—Use in women of childbearing potential only when potential benefits outweigh possible risks.
Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.
Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-four patients, it was not possible to state that the dysfunction was or was not drug induced.
Usual Adult Dosage: Two tablets q.i.d.
Supplied: Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: **1.** Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 1955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, F.N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: New Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboratories, Inc.

† U.S. Patent No. 2,895,877

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Trademark

Each capsule contains 50 mg. of Dyrenium* (brand of triamterene) and 25 mg. of hydrochlorothiazide.

Neither inconvenient potassium supplements nor special K+ rich diets needed as a rule. Just 'Dyazide' once or twice daily for maintenance.

Two prime reasons patients drop out of hypertensive therapy are (1) the patient failed to understand directions, and (2) the regimen was overly complicated. Dosage is simple with 'Dyazide', easily understood, once or twice daily, depending on response. There's no need to complicate the regimen with potassium supplements or unwieldy potassium-rich diets.

TO KEEP BLOOD PRESSURE DOWN AND KEEP POTASSIUM LEVELS UP

Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

Indications: Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: **Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired.** Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. **Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently—both can cause potassium retention and sometimes hyperkalemia.** Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias, icterus, pancreatitis, and xanthopsia have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

SK&F CO.
Carolina, P.R. 00630
Subsidiary of
SmithKline Corporation

"Gentlemen, congratulations are in order."

"A.H. Robins asked me to compare the banana flavor of their Donnagel® -PG with the real thing and, by jove, I couldn't tell the difference. Not even in sip-by-sip comparison. Amazing!

"There's no unpleasant paregoric taste because there's no paregoric. Clever, wouldn't you say? Instead, A. H. Robins uses the therapeutic equivalent, powdered opium, to promote the production of formed stools and lessen the urge. And Donnagel-PG also provides the demulcent-detoxicant effects of kaolin and pectin, plus the antispasmodic benefits of belladonna alkaloids.

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"May I propose a toast?"

A·H·ROBINS

A H Robins Company, Richmond, Virginia 23220

Donnagel®-PG. Ⓥ

Donnagel with paregoric equivalent
Each 30 cc. contains:

Kaolin	6.0 g
Pectin	142.8 mg
Hyoscyamine sulfate	0.1037 mg
Atropine sulfate	0.0194 mg
Hyoscine hydrobromide	0.0065 mg
Powdered opium, USP (equivalent to paregoric 6 ml.) (warning: may be habit forming)	24.0 mg
Sodium benzoate (preservative)	60.0 mg
Alcohol, 5%	

Ⓥ Available on oral prescription or without prescription in compliance with applicable state and local law

Robitussin
Robitussin A-C
Robitussin-DM
Robitussin-PE
Robitussin-CF
Cough Calmers

A·H·ROBINS

IN COUGHS OF COLDS, 'FLU,' AND U.R.I.: CLEAR THE TRACT WITH THE ROBITUSSIN® LINE

Fall and winter coughs are back. Time to help clear the lower respiratory tract with the five Robitussins and Cough Calmers. All contain glyceryl guaiacolate, the efficient expectorant that works systemically to help increase the output of lower respiratory tract fluid. The enhanced flow of less viscid secretions soothes the tracheobronchial mucosa, promotes ciliary action, and makes thick, inspissated mucus less viscid and easier to raise. Available on your prescription or recommendation.

For unproductive coughs

ROBITUSSIN®

Each 5 cc. contains:

Glyceryl guaiacolate	100 mg.
Alcohol, 3.5%	

For severe coughs

ROBITUSSIN A-C® Ⓒ

Each 5 cc. contains:

Glyceryl guaiacolate	100 mg.
Codeine phosphate	10.0 mg.
(warning: may be habit forming)	
Alcohol, 3.5%	

Non-narcotic for 6-8 hr. cough control

ROBITUSSIN-DM®

Each 5 cc. contains:

Glyceryl guaiacolate	100 mg.
Dextromethorphan hydrobromide	15 mg.
Alcohol, 1.4%	

Robitussin-DM in solid form for "coughs on the go"

COUGH CALMERS®

Each Cough Calmer contains:

Glyceryl guaiacolate	50 mg.
Dextromethorphan hydrobromide	7.5 mg.

Clears nasal and sinus passages as it relieves coughs

ROBITUSSIN-PE®

Each 5 cc. contains:

Glyceryl guaiacolate	100 mg.
Phenylephrine hydrochloride	10 mg.
Alcohol, 1.4%	

MEET THE NEWEST MEMBER OF THE LINE

Comprehensive decongestant action helps control cough and clear stuffy nose and sinuses. Non-narcotic.

ROBITUSSIN®-CF

Each 5 cc. contains:

Glyceryl guaiacolate	50 mg.
Dextromethorphan hydrobromide	10.0 mg.
Phenylpropanolamine hydrochloride	12.5 mg.
Alcohol, 1.4%	

Select the Robitussin® formulation that treats your patient's individual coughing needs:	Expectorant-Demulcent	Cough Suppressant	Long-Acting (6-8 hours)	Nasal, Sinus Decongestant	Non-Narcotic
ROBITUSSIN®	●				●
ROBITUSSIN A-C®	●	●			
ROBITUSSIN-DM®	●	●	●		●
ROBITUSSIN-PE®	●			●	●
ROBITUSSIN®-CF	●	●		●	●
COUGH CALMERS®	■	■	■		■

A. H. Robins Company, Richmond, Va. 23220

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cefazolin sodium
Ampoules, equivalent to 1 Gm. of cefazolin

Lilly

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400380

Malpractice Crisis—Tip of an Iceberg

We have developed and accepted a stupid way of running things in these United States. Today, most of the important decisions about the conduct of our society are made by the court. The people who have proposed and promoted the concepts, and the lawmakers who have taken the action, are rarely involved in the implementation. So in Boston, Judge W. A. Garrity is saddled with declaring the procedures to integrate the public school system, just as Judge William Doyle was delegated the sole authority for redistributing the school children of Denver in the face of a vote of the people to maintain their neighborhood schools. A few days ago, after volumes of high level discussion by lawmakers, physicians, and theologians, and after gargantuan campaigns by other concerned people, a decision that defines how the abortion law should operate was made by a jury picked because of their previous non-involvement and perhaps lack of awareness — who needed the definition of *viable.* These are examples of hundreds of laws and actions which have been formulated by participation of many kinds of knowledgeable people, the implementation of which comes to rest with individuals who had no previous involvement with the issue and who usually do not want the job. The system seems to be set up so that interpretation and implementation is forfeited to the courts, which in turn are designed to have the judgments made by the previously uninformed.

The crisis in malpractice insurance results from this same method of operation of our laws. A few years ago, the lawmakers for great political advantage decided that health care was a right. The step to inference that good health is the usual and logical expectation was automatic. Then it followed that a procedure which did not produce good health obviously was denial of this right and was grounds for legal redress. The courts then became busy deciding if people's rights to good health had been compromised.

Of course there are contributing factors to development of the malpractice crisis. But to place a major blame upon the legal profession is more emotional than rational. There are no more greedy or unprincipled lawyers than before. The ethics of the legal profession have not changed. Nor can the blame be placed on the courts for the gigantic size of malpractice judgments. Huge judgments are not restricted to malpractice claims. The fabulous judgments merely reflect our times in which there are fabulous payments for the right bell to ring in a TV show, fabulous salaries for professional athletes, fabulous prizes for sporting events, and fabulous expenditures by government. And let's be objective, an occasional exorbitant fee of a colleague is long remembered.

There are those who suspect that Wilbur Cohen, Ted Kennedy, and the others planned for this crisis in liability coverage by the guarantee of health care through the medicare bill, and that they knew that this problem would force the physicians into socialized medicine. Although the liberals would welcome any kind of pressure on the doctor, total socialization would not stop the increase in malpractice claims. The more people that are guaranteed good health by the government, the more there will be who believe that they have a right for compensation for a less than good medical result. It is hard to believe that the mere fact that the program is government-owned will immunize it and the program from attacks by the aggressive, intelligent, and enterprising American lawyer.

No, the crisis in malpractice insurance is just one more problem resulting from the way we allow our total system of government to work. The people who are selected or appointed to handle our problems only do part of their job. They forfeit the responsibility of interpretation and implementation of their actions to the courts. Nevertheless, the solution of the problem of medical liability insurance would seem to be with these people who make the laws — the congress and the legislatures. And we must convince the lawmakers that they should spend more time figuring out the implementation and the potential problems of their laws. If they continue to buck part of their job to the judges and the courts, at least they should raise the pay of the judges. The congress sees that the salaries and fringe benefits of its membership are currently increased — federal judges have been at $40,000 since 1969.

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Intravenous hyperalimentation*

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We are an overfed society and probably most people could withstand and benefit from a few days of negative nitrogen balance! However, when considering intravenous hyperalimentation, IVHA, the physician is confronted with a depleted or bankrupt nutritional state. The ultimate goal is to achieve restoration to a positive caloric and nitrogen balance and physical well being. IVHA must be considered one of the most valuable adjuncts and modalities of treatment in a variety of difficult clinical problems which present a negative nitrogen balance. Although many refinements remain to be added, and more precise understanding of metabolic requirements and responses to treatment need to be delineated, IVHA is a practical means of effective nutritional support.

Special surgical nutrition is needed only in select patients. The average patient with normal nutritional reserves can withstand the reduced caloric and protein intake of an acute illness or massive surgery. However, occasionally, a patient requires special nutritional support to recover, and many times it may be lifesaving.[1] The decision to give nutritional support is dependent upon the degree of nutritional reserve and the rate of nutritional depletion. The nutrition may be supported by two routes — oral or parenteral. Since we will address ourselves to the parenteral route, suffice it to say that one may supplement diet orally with special dietary additives, with special diets, (that is, medium chain triglycerides as used in the malabsorption syndrome) or with a completely soluble elemental diet (Vivonex).

An example of pathologic caloric expenditure is peritonitis, which may require 4000-5000 calories/day. The patient with burns or other severe trauma may require as much as 8,000 to 10,000 calories/day. Theoretically, the human body has approximately 165,000 utilizable calories of which about 40 per cent (65,000) can be expended before death ensues. Therefore, one can "starve to death" in 6-10 days.

The basic problem encountered with intravenous feedings in the critically ill patient is that he requires approximately three fold that of normal nutrition, and this need is even greater with fever, infection, tissue destruction, trauma, etc. In these patients only about one-eighth to one-sixth of their caloric requirements are met with the usual 5% Dextrose crystalloids. The balance is obtained by breakdown of body glycogen, fat, and protein (catabolism). In the healthy patient there is no problem for the short term. However, in the long term debilitated patient, "clinical starvation" occurs. This cannot be reversed with the usual crystalloids and more effective nutritional support, such as IVHA is required.

Total IVHA completely bypasses the gastrointestinal tract and is dependent on an infusion of carbohydrate as the source of calories and an infusion of protein hydrolysate or a pure synthetic amino-acid solution (McGaw 8.5% freamine solution) as the source of nitrogen. The protein hydrolysates are a less than perfect source of nitrogen because they contain peptides which cause sensitivity reactions. Their amino-acid patterns are not ideal since nitrogen content is too low, and therefore the freamine solution is generally better.

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History:

Quest for an effective surgical parenteral alimentation began almost a half century ago. Cole and Elman[2] in the early 40's were the first to suggest 5% amino-acid infusion (aminosol), which was helpful for the short term but couldn't sustain a positive nitrogen balance over the long haul. In the 1950's intravenous fat emulsions, such as cottonseed oil, became available, and although they were good for the long term caloric input, too many serious side effects were noted, and they had to be abandoned. However, new, exciting and better tolerated fatty emulsions are being developed in the Scandinavian countries, and hopefully these may soon be available. In the early 1960's large volumes of 10% Dextrose were used. These overloaded the kidneys (osmotic diuresis) and caused fluid retention and increased cardiac strain and for other than short term use they were ineffective. Shortly, diuretics were added to the large volume 10% Dextrose solutions, and this helped with renal overload, but electrolyte balance and positive nitrogen balance were difficult to maintain, and this approach was eventually discontinued. Stanley Dudrick[1] in 1967 showed subclavian vein delivery of hypertonic and hyperosmolar solutions was well tolerated since the high flow rate rapidly diluted these solutions to isotonicity and thus obviated venous inflammation and venous thrombosis that occurred in peripheral veins.

It has long been known that for normal protein synthesis 120 to 150 non-protein (carbohydrate) calories are required as the source of energy for each 1 gram of parenteral nitrogen. Otherwise, the amino-acid solutions themselves would become deaminated or oxidized for energy. Dudrick must be credited with working out the details of the safe delivery of the admixture of 50% Dextrose (500 cc.) and 8.5% proteins (500 cc. freamine) which cannot be tolerated by the peripheral veins. The IVHA solution supplies essential and non-essential amino-acids, concentrated carbohydrate solution, vitamins and electrolytes. It provides total parenteral nutrition capable of maintaining normal growth and development and positive nitrogen balance. IVHA is dependent upon the age and clinical state of the patient. Infants, for example, require 125 calories/kg./day and 0.7 gm. N_2/kg./day; adults require 50 calories/kg./-day and 0.2 gm. N_2/kg./day. In 1967 Dudrick et al.[1] utilized IVHA in a one-month-old infant with congenital intestinal anomalies and multiple surgical procedures for a period of 22 months, and the child at the end of that period showed normal growth and development and had complete recovery. In 1969 total IVHA was used for a one year period in an adult with multiple surgeries and multiple fistulae, and he, too, had a complete recovery.

Advantages

There are numerous advantages of total or supplemental IVHA. (1) It removes the added burden of inadequate nutrition. (2) It promotes tissue synthesis and enhances wound healing. (3) It supports anabolism (positive nitrogen balance) under conditions usually associated with catabolism. (4) IVHA vastly increases the surgeon's capabilities of dealing with generally catastrophic complications previously thought to be irreversible. Finally, (5) positive nitrogen balance may occasionally be achieved with renal failure, impaired liver function and/or complete disruption of G.I. tract.

Indications

Patient who cannot eat: IVHA is valuable in the patient with long standing obstruction or massive bowel resection where oral feeding is impossible or inadequate and total nutrition is needed. In the patient with a massive bowel resection its use may help the GI tract to adapt to its new length. It may be indicated in the infant who has congenital anomalies as duodenal atresia, especially in neonatal period.

Patient who should not eat: Hyperalimentation hastens spontaneous closure of enterocutaneous fistulae. Many patients with inflammatory lesions, as ulcerative colitis or regional enteritis, go into remissions with IVHA.

Patient who cannot eat enough: Patients with hypermetabolic states, severe catabolism, septicemia, fever, shock, extensive trauma, indolent intestinal ulcer, multiple injuries, and sepsis can be given extra support with this modality. The average nitrogen loss from feces, urine, sweat, etc., equals 13-15 grams per 24 hours and in hypermetabolic states this is increased to 20-25 grams nitrogen. It is apparent then, if 1,000 ml. of IVHA supplies 6 grams nitrogen, these patients may require between 3500-4000 IVHA per 24 hours to keep in positive nitrogen balance. Also IVHA may be used to prepare the greatly debilitated patient for massive surgery, such as operation for long standing pyloric obstruction, esophageal carcinoma, ulcerative colitis, carcinoma of the lung, and carcinoma of the stomach.

Patient who will not eat enough: Psychiatric patients and persons with anorexia nervosa or hyperemesis gravidarum, or others who refuse to eat may be fed by IVHA.

Finally, there are a number of medical conditions where IVHA may prove beneficial. It is used in patients with renal failure, and it may produce reversal of hyperammonemia and anasarca in liver failure. IVHA opens up new horizons to study bizarre nutritional and metabolic problems by total control bypass of the gut as components of diet can be manipulated under the most strict laboratory conditions.

Technic and Protocol

The hyperalimentation solution is administered through a subclavian line. Introduction of the subclavian catheter is now a standard procedure. The IV tubing and dressings about the puncture site should be changed at least every other day and Neosporin ointment placed around the puncture site. The 50% Dextrose and freamine solutions should be mixed by the pharmacist under a hood with laminar flow and not by staff nurses. One should avoid the withdrawal and injection of blood products through the subclavian line.

IVHA solution is hyperosmolar (2000-2500 milliosmols/kg/L as compared to blood with 250-300 milliosmols/kg/L). The infusion of this hyperosmolar solution must be at a constant rate since the kidney has difficulty in adjusting to sudden carbohydrate overload of hypertonic solution and responds with carbohydrate (osmotic) diuresis with increase in potassium loss. Rapid infusion may cause hyperosmolar syndrome (mental confusion, unconsciousness, etc.) especially in patients with chronic uremia and also in patients with known carbohydrate intolerance. Carbohydrate utilization is 0.4-1.2 gm/kg/hr and constant slow IV rate facilitates efficient glucose utilization by cells and maximum sparing of amino-acid for protein synthesis. Constant slow rate also prevents hyperglycemia which can cause increase of glucosuria and osmotic diuresis. Occasionally some patients can't tolerate more than 800 ml. per 24 hours without osmotic diuresis. Therefore, the rate must be tailored for each patient and/or crystalloids need to be added via a separate intravenous route. The constant rate of infusion of IVHA solution is mandatory. Exercise is important to anabolism, and therefore, when possible, the patient should receive physical therapy and ambulation.

A typical protocol for the average adult for total or supplemental IVHA is as follows:

1. Start with 1000-2000 ml. balanced freamine solution per 24 hours infused at a constant rate (40-80 cc./hr.). The rate can be increased up to 2500-3000 as tolerated over a period of 7-10 days with an average increment of 250 cc./day.

2. Baseline laboratory: CBC, UA, BUN, magnesium, creatinine, blood sugar, liver profile, urine sodium and potassium, serum osmolality, calcium, and phosphorus.

3. Daily electrolytes until stable, then every 3-5 days.

4. BUN, blood sugar, CBC, serum osmolality, every three days and as necessary.

5. Typical additives per 1000 ml. are as follows (as recommended by Walter Reed Hospital):
   a. 25 meq NaCL/1000 ml.
   b. 20 meq NaAcetate/1000 ml. $NaHCO_2$ can be substituted if acidosis or hyperchloremia exists, and if no calcium is used.
   c. 20 meq K^+H Acetate/1000 ml.
   d. 20 meq K^+H Phosphate/1000 cc.
   e. 1000 u Heparin/1000 cc.

6. 10 ml. 10% Calcium gluconate is added to approximately every third liter.

7. 8.1 meq $MgSO_4$ (1 cc. of 50% solution/1000 ml) is given every third or fourth liter depending upon the serum level of magnesium.

8. One ampule MVI (fat and water soluble vitamin)/1000 mo. (not to exceed 1 amp/24 hours) prevents development of A and D hypervitaminosis over a period of several weeks.

9. Folic acid can be added in dosage of 0.5-1.5 mg. daily IV push in a separate IV line or 15 mg. IM push/week.

10. Vitamin B12, 1000 micrograms IM every month.

11. Aquamephyton (Vitamin K) may be given if needed if gut sterilizing antimicrobics are being used.

12. Intake and output: patient should be NPO unless IVHA is supplemental.

13. CVP only as necessary.

14. Weigh patient daily to check fluid accumulation.

15. Clinitest for sugar and acetone every six hours.

16. Insulin subcutaneously (not in IVHA solution) as follows:
   Trace—2+ clinitest: 0 insulin
   3+ clinitest: give 3-5 units regular insulin to geriatric and non-diabetic patients. (diabetic may be sensitive to insulin)

17. Add antimicrobics, blood colloids, etc. in separate IV lines.

18. Do not withdraw blood from subclavian line.

19. If possible avoid calcium phosphates and magnesium when sodium bicarbonates are used as source of sodium, as they are incompatible.

20. Tracer elements (copper and zinc) are probably best added with plasmanate every two-three weeks.

21. The milipore filter which was previously used is now being replaced by an in-line SAIF filter (0.45 micron). This filters all particulate matter and bacteria except Pseudomonas. This latter organism requires a filter 0.25 microns, which size filter requires pressure to deliver IVHA.

22. IVHA solution is not stable, and therefore, it should not hang for more than 24 hours.

23. Miscellaneous adjunctive care: GI decompression, local wound care, I & D of abscesses, correction of blood and fluid losses as required.

Precautions and Complications:

Fifty per cent carbohydrate solution is contraindicated in intracranial or intraspinal hemorrhage or in delerium tremens if the patient is already dehydrated. Freamine solution is contraindicated in anuria, and hepatic coma, and it should be used with caution in patients who are oliguric where BUN and creatinine may be increased. It should be used with caution in patients with hepatic insufficiency as it may cause increase in blood ammonia.

Phosphorus blood levels drop predictably and decrease can cause peripheral type of cyanosis because of the increased affinity of the RBC's for oxygen. This is obviated by using 18-25 meq of Phosphate/1000 ml. of IVHA. The phosphates are especially required and needed in the early phase of IVHA. Potassium and magnesium are important as intracellular cations. The phosphates are important intracellular anion and are important for deposition of protoplasm and formation of lean body tissues. Sodium chlorides and calcium are principally extracellular electrolytes (ions). Hypophosphatemia and hypophosphaturia are important aberrations that should be watched for carefully.

Early weight gain denotes water, and this is the initial correction of the dehydration present in catabolism. Wound healing can be noticed soon after start of therapy. "Hyperalimentation euphoria" is a state of well being as homeostasis is regained, i.e., temperature down, pulse normal and all the pluses and minuses are corrected.

The most important complication of IVHA is sepsis, particularly with candida albicans (fungemia).[3] Although few fungi organisms are dangerous, with long term indwelling catheters increase in number of organisms causes serious sepsis. Goldman, et al. showed that although IVHA solution is hypertonic and acidic (not conducive to bacterial and fungal growth) organisms may proliferate in these solutions at room temperature. Therefore, these solutions should be utilized as quickly as possible after preparation. Treatment for sepsis is to remove the subclavian catheter and culture the tip for Candida. Then one should consider starting Amphotericin B, a very toxic drug. However, occasionally simple removal of the infected subclavian catheter alone will clear the infection. Occasionally, some advocate intermittent Amphotericin B into infusion line prophylactically. Pyogenic bacterial sepses are treated with the appropriate antimicrobics.

Another serious complication is the "hyperosmolar syndrome" (non-ketotic coma) especially in elderly and diabetic patients. It is characterized by mental confusion, coma, dehydration, hyperglycemia (blood sugars may be between 500-1500 mg%), increase in serum osmolality. There is peculiar lack of ketonemia. This complication may be occasionally caused by rapid infusion of the IVHA. It occurs more frequently in patients with chronic uremia and carbohydrate intolerance. In hyperosmolarity, osmotic diuresis is present, and the syndrome is treated with increase in hypotonic solutions such as 5% Dextrose in 1/4 strength saline by way of a separate IV line.

Occasionally prolonged IVHA may tax the pancreatic islet cells, insufficient endogenous insulin is produced, and the patient may need insulin by subcutaneous route to control the hyperglycemia. Or the reverse may occur, and the patient on prolonged IVHA may be very sensitive to insulin (i.e. with high carbohydrate stimulation, islet cells gradually produce more endogenous insulin and the usual dose of exogenous insulin may cause hypoglycemia and death). The patient who has the IVHA suddenly discontinued must be watched for sudden hypoglycemia since the islet cells may lag in their decrease of endogenous insulin production resulting in high endogenous insulin on board, and the patient may become hypoglycemic and need 5% Dextrose crystalloid solution for a while after discontinuation of IVHA.

There is a need for increased potassium as anabolism is reached, since potassium moves back into intracellular compartment and the usual 30-40 meq KCL/1000 ml may not be sufficient. Also, in osmotic diuresis, stress, infection, shock, etc., the patient may need more potassium.

Fever and/or rash is occasionally caused by the peptides particularly when Aminosol or the Casein hydrolysate are used to prepare the protein solution. Dudrick[1] recently stated that many starvation patients develop skin changes from lack of lipid alimentation and may need to be given fatty acid intravenously. This can be achieved by infusing blood from a patient who has had a high fatty meal and whose blood is then spun down recovering the fat-laden supernatant fluid.

Summary

The history, advantages, indications, technic, and complications of intravenous hyperalimentation have been presented. Inability to eat should no longer be considered an unavoidable factor in the fatal outcome of a complicated surgical problem.

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Hydrocele of the canal of Nuck

A report of two adult cases

Robert A. McElfatrick, MD and William B. Condon, MD, Denver

In the late eighteenth century, Scarpa, in his book, "Tumors of the Spermatic Cord", described a cystic tumor in the female inguinal canal as a "hydrocele of the canal of Nuck".[1] Since then, additional titles such as "hydrocele muliebris" and "hydrocele in the female" have also been applied in a general way to all cysts occurring in the inguinal region of the female.[2] Although the finding of hydrocele is not uncommon in female infants, its occurrence in the adult is considered rare. Two cases in adult females are presented not only for their rarity, but also to show how clinically the entity can be mistaken for incarcerated or strangulated hernia.

CASE REPORTS

Case 1: A 33-year-old white female was admitted to the hospital with a two day history of a painful swelling in the left groin. A lump which had been present in the groin for about five years had previously been diagnosed as a hernia. On the day prior to admission, the swelling in the groin increased in size and became painful. There was associated nausea and one episode of vomiting.

On examination, the left inguinal canal contained an extremely tender swelling which extended into the labia majora. The overlying skin was red and edematous. There was no swelling on the opposite side. White cell count was 9,300 with 87 per cent neutrophils; other laboratory tests were within normal range. Radiologic examination of abdomen showed normal gas pattern. The patient was scheduled for surgery with preoperative diagnosis of incarcerated inguinal hernia.

At operation, a multi-loculated hydrocele was found in the inguinal canal, which extended into the labia majora. This was resected and an associated indirect inguinal hernia repaired.

Pathologic examination showed an irregular shaped, multi-loculated cystic mass which on microscopic study showed subacute inflammatory changes and fibrosis adjacent to a serous lined cyst wall. Antibiotic coverage was given postoperatively and the patient was discharged on the fourth postoperative day.

Case 2: A 41-year-old nurse was seen in the emergency room with a painful lump in the right groin. Although she had been actively involved in heavy lifting one week earlier, there was no unusual strain. She first noticed this painful lump two days previously. There was no associated nausea or vomiting.

On examination, there was a 3 cm. tender, irreducible mass in the right inguinal canal. There was no impulse on coughing. The abdomen was soft with normal bowel tones. There was no evidence of an inguinal or femoral hernia on the left side. All laboratory tests, including the white cell count, were within the normal range. A preoperative diagnosis of incarcerated inguinal hernia was made and the patient was admitted for surgery the next day.

At operation, a 4 cm. x 3 cm. multi-locular cystic mass occupied the inguinal canal adjacent to the round ligament. There was no indirect hernia. This mass was freed from its attachments and excised with the round ligament, whose muscular coat seemed to integrate with the walls of the cyst. The end of the round ligament was anchored and the inguinal floor was repaired.

Pathologic examination showed a 4 cm. x 3 cm. x 2 cm. cystic structure filled with clear yellowish fluid, and lined with mesothelium. The patient was discharged on the fifth postoperative day after an uneventful course.

Discussion

Analogous to the processus vaginalis in the male, the canal of Nuck is a tubular process of peritoneum, extending alongside the round ligament into the inguinal canal. As in the male infant, this peritoneal lining obliterates during the first year of life. If it persists, and the connection to the peritoneum is closed, the child develops a hydrocele of the canal of Nuck. Statistically, the obliteration is more likely to be complete in females, who have a lower total incidence of herniae, but a higher incidence of bilateral herniae.[3] Despite the high incidence of bilaterality, all reported cases of hydrocele in adult females are unilateral.[4] Although hydroceles in infants are thought to be due to persistent patency of this peritoneal process in the inguinal canal, in adults they are believed to result from slower absorption than secretion of fluid.[5] The most common type of hydrocele of the canal of Nuck corresponds to the encysted hydrocele of the cord in the male. Therefore, there is no communication between the cyst and the peritoneal cavity. The adult hydrocele may vary in size, is usually multi-locular and can be located anywhere from the internal ring as far as the labia majora. A second type of hydrocele does communicate with the peritoneal cavity and this corresponds to the congenital hydrocele in the male. Hourglass hydroceles are occasionally reported, in which the upper sac located intra-abdominally communicates with a lower sac in the inguinal canal.[1]

Histologically, these hydroceles are lined with a pavement epithelium similar in all respects to cells lining the peritoneal cavity. Smooth muscle may be present in the wall but is not a constant finding.

Comment

The diagnosis of hydrocele in the adult female may present difficulty. A small hydrocele may be so placed in the inguinal canal of an obese patient that adequate palpation and transillumination cannot be employed. The apparent reducibility of a mass and an impulse on coughing cannot be relied upon to differentiate between hydrocele and hernia, because herniae are often an associated condition.[6] However, those hydroceles which do extend through the external ring into the labia majora do afford easier palpation and can be transilluminated.

Hydroceles which have remained asymptomatic for months or years occasionally develop symptoms resembling incarceration or strangulation. Local inflammation of the sac and the surrounding skin seems to have been responsible for pain, nausea and vomiting noted in Case 1. In a thin patient, the presence of a tense, fluctuant swelling, either in the inguinal canal or extending through the external ring, which developed slowly without any known cause and which gives no impulse on coughing will suggest a hydrocele.

Summary

(1) Two cases of hydrocele in the adult female are reported, both of which presented with symptoms resembling incarcerated inguinal hernia.

(2) Because of the frequent association of inguinal hernia, the correct diagnosis may not be made until the mass is surgically exposed.

ACKNOWLEDGMENT

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Splenic trauma*

Three Pronged Diagnosis

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Accuracy in evaluation of splenic injury has increased through use of peritoneal lavage, splenic scan and arteriography. These technics are discussed and illustrated with three cases.

RUPTURE OF THE SPLEEN is the most common serious intra-abdominal injury from blunt abdominal trauma.[1] The mortality of treated cases is approximately 1 per cent, increasing to 80 to 100 per cent in untreated cases.[2] Splenic trauma can result in several types of injury, each having its own presentation. Capsular laceration results in rapid, extensive hemorrhage in approximately 85 per cent of cases. In the remainder the capsule remains intact, and a contained hematoma forms, destined to rebleed massively sometime in the next two weeks. Rarely the injury and hemorrhage is confined by adhesions and omentum to the left upper quadrant, and years later, in some of these patients, abdominal pain, weight loss, and a left upper quadrant mass may suggest neoplasm or occult splenic rupture.[3]

In the past, diagnosis of patients with splenic trauma rested on a careful collation of frequently subtle clinical findings followed either by surgical exploration or prolonged observation. Whatever the choice, it was frequently wrong in the sense that many patients were explored who had no significant injury while others were observed who should have been operated upon immediately. Still other patients were unnecessarily hospitalized for suspected injury that had not occurred.

Peritoneal lavage, scan and arteriography are technical additions to the evaluation of blunt abdominal trauma which have been particularly useful in reducing morbidity and length of hospital stay. Since the spleen is the organ most commonly injured, it is appropriate to discuss the application of these technics in this organ alone. A more general application to the evaluation of blunt abdominal trauma is nevertheless suggested.

CASE REPORTS

Case 1: A 22-year-old male, Utah Ski Team member, was seen in the University Hospital Emergency Room, complaining of left chest and abdominal pain. He had fallen on a mogul while skiing, landing on his left chest and knocking his wind out. He subsequently felt light-headed and had persistent discomfort of left chest and upper abdomen.

On physical examination, vital signs were within normal limits. The abdomen was not distended and the bowel sounds were normal. There was minimal left-sided pain with forceful left rib cage compression. There was some tenderness in the left upper quadrant with radiation to the left thorax and tenderness in the right upper quadrant with radiation to the right shoulder. There was, however, no abdominal guarding. By laboratory examination, hematocrit was 52, white count was 15.5, and urinalysis was within normal limits. Chest x-ray and rib films were normal. The patient was sent home to return if his symptoms worsened. That evening the patient returned with a story of increasing left upper quadrant pain and one episode of syncope. On physical examination, vital signs were normal. The bowel sounds were decreased and there was left upper quadrant tenderness without guarding or rebound. The hematocrit had fallen to 42 and the white count was 15.7. Urinalysis was still normal. Peritoneal lavage returned gross blood on introduction of the catheter. At laparotomy, the patient had a 2 cm. laceration in the superior pole of the spleen.

COMMENT:

The housestaff was fortunate in this instance to make a diagnosis before the patient became hypotensive. However, the patient did have "worrisome abdominal findings" when first seen and a stricter application of the indications for peritoneal lavage almost certainly would have resulted in an earlier diagnosis and less risk for the patient.

Peritoneal Lavage

The purpose of peritoneal lavage is to rule rapidly in or out virtually any form of major intra-abdominal injury. Retroperitoneal injury, as of the genitourinary tract or duodenum[4] are not delineated. The indications for peritoneal

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lavage are:[4-7] (1) patients who have sustained blunt trauma with subsequent (a) worrisome abdominal findings, (b) unexplained hypotension, (c) chest injuries, e.g. rib fractures with equivocal findings of peritoneal irritation, or (d) head injuries and unconsciousness where potential for other injury is present, and (2) patients with stab wounds where signs and symptoms are minimal and observation appears to be an acceptable course. The contraindications to peritoneal lavage include: (1) multiple previous abdominal operations, (2) pregnancy, (3) grossly dilated bowel, and (4) gunshot wounds.

The usefulness of the technic is highlighted by these two observations from a published study. In a group of blunt trauma victims who had abdominal findings for which laparotomy would have been necessary to rule out major injury, 60 per cent were successfully managed without laparotomy because of negative lavage results. Conversely, of those patients who would otherwise have been observed, 20 per cent underwent laparotomy because of positive lavage results and thereby received appropriate visceral repair.[4] The incidence of false positive results has ranged from 0.7 per cent to 3.5 per cent and false negative results, from 0.5 per cent to 3.1 per cent.[4-6] The complication rate has varied from 0.5 per cent to 4.5 per cent, and no mortality has been reported.[4,5]

The technic of peritoneal lavage involves the introduction of a standard peritoneal dialysis catheter into the abdominal cavity. The bladder is first catheterized, and then the lower mid-abdomen is prepped. A small, midline, skin incision is made one-third of the distance from the umbilicus to the symphysis pubis. If the patient is thin, the midline fascia is also incised. The catheter, with stylet, is pushed into the peritoneal cavity, and the stylet removed. Here, a syringe is attached and an attempt made to aspirate blood or fluid. If none is obtained, the catheter is pushed further into the peritoneal cavity in the direction of the pelvis. The dialysis catheter is then taped to the abdominal wall, connected to a standard I.V. tubing, and a liter of normal saline or balanced electrolyte solution run into the abdominal cavity. The volume is appropriately decreased in children (10 cc. per kg.). The empty I.V. bottle is next lowered to the floor and fluid siphoned out of the peritoneal cavity. Variations in the type of catheter or anatomic location for placement are acceptable under certain circumstances, but they have generally been attended by a higher rate of complications and technical difficulties.[4-6]

Interpretation is not difficult. The majority of positive findings are based on a grossly bloody returned fluid. For purposes of definition, more than 20 cc. of blood per liter of lavage fluid is considered positive and an indication for immediate surgical exploration. This correlates well with a red blood cell count of 100,000/mm.^{3} and a hematocrit of 1, or loss of the ability to read newsprint through the fluid in the tubing. Lavage return is also considered positive if it contains greater than 500 WBC/mm,^{3} 100 units of amylase/100 cc, bacteria or detectable bile. Unless other findings are impressive, negative lavage results obviate the need for further diagnostic workup and are sufficient assurance that no major intra-abdominal injury has occurred.[4-7]

Case 2: A 17-year-old male was admitted to a rural hospital with complaint of left thoraco-abdominal pain subsequent to a left side injury in an auto-truck accident on the same day. On physical examination, the blood pressure was 90/60. There was an abrasion of his left thorax and left ankle. Thoraco-abdominal examination was otherwise normal. Hematocrit was 40, and white count was 12,000. Urinalysis was normal, and chest x-ray was reportedly normal. The next day, the patient was eating a regular diet and had a normal bowel movement. The bowel sounds were normal, but his abdomen seemed generally more tender with maximal tenderness in the left upper quadrant. On the second day following admission, the patient complained of generalized abdominal pain. Physical examination was unchanged except for absent bowel sounds. Hematocrit was 37 and white count was 8.9. The patient was transferred to the University Hospital. On arrival at the University Hospital, the patient's blood pressure was 120/80 and pulse was 88. Bowel sounds were absent. There was general abdominal tenderness with spasm of left rectus and flank muscles. There was some evidence of peritoneal irritation on rectal examination. Hematocrit was 33, and white count was 7.8. Peritoneal lavage was equivocal returning 10 to 15 cc. of blood per liter of fluid. Plain film of the abdomen showed an absent left psoas shadow. A splenic arteriogram, done the same day, was reported as normal. The diagnostic impression was that of retroperitoneal hemorrhage.

On the third day of admission, the patient had improved clinically. The abdomen was less tender and bowel sounds were hypoactive. The hematocrit, however, had fallen to 27 and the white count was 6.8. The patient was given two units of whole blood resulting in a hematocrit rise to 36. Over the next four days, the patient improved clinically, ambulating and eating, and his hematocrit remained stable. On the eighth post-accident day, an enlarging left pleural effusion was tapped for 650 cc. of serosanguineous fluid, subsequent to which the patient began to complain of mild left upper quadrant pain. Two days later, the patient was still complaining of left upper quadrant pain of increasing frequency.

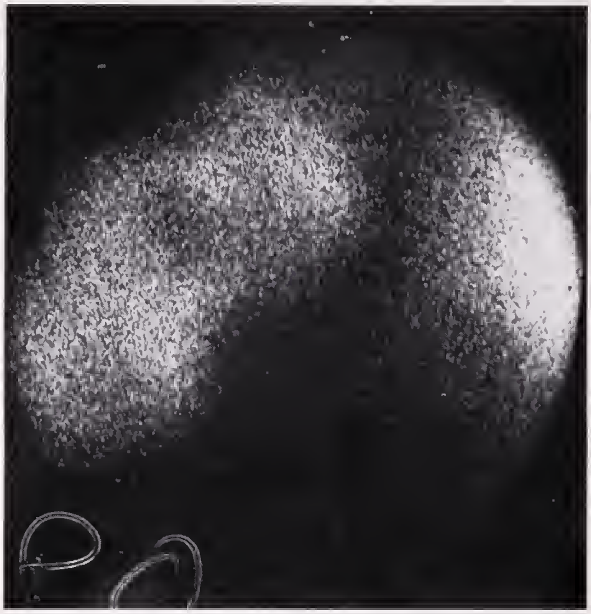

Fig. 1. Left posterior oblique view of spleen in case #2 illustrating filling defects in the superior and inferior poles.

A splenic scintiscan was read as abnormal (Fig. 1). The splenic arteriogram was reviewed and read as abnormal also. At operation there were dense adhesions of omentum to the inferior and medial aspects of the spleen and of the spleen itself to the laterai wall of the abdomen. There was around 200 cc. of dark blood in the peritoneal cavity. Splenectomy was carried out.

COMMENT:

The patient might well have been explored two days after admission except that he had an equivocal lavage and the arteriogram, which did not include selective splenic artery injection, was read as normal. An arteriogram was obtained prior to liver-spleen scan, because we were not, at that time, sure of the reliability of scans in diagnosing abdominal trauma. As it turned out, the scan was the definitive study which forced review of the arteriogram and subsequent laparotomy.

Scans

Isotope scans are surprisingly helpful in the evaluation of blunt abdominal trauma and comprise the second step in ruling in or out injury of spleen and liver. Although more expensive and slightly more specific than peritoneal lavage, the isotope scan may disclose an occasional hemorrhage entirely contained in the spleen.[8] The isotope scan is, moreover, cheaper than arteriography and noninvasive. For the above reasons, in patients with a negative lavage and persistent left upper quadrant pain, as well as patients with equivocal lavage results where splenic injury is a possibility, a liver-spleen scan should be performed.

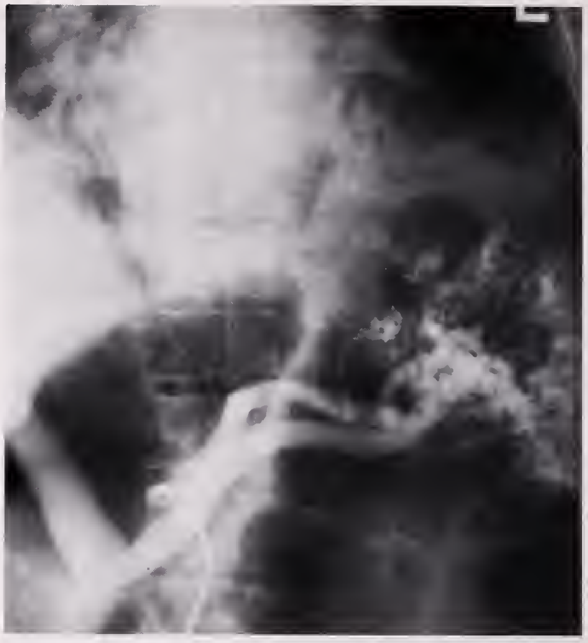

Fig. 2. Selective splenic arteriogram demonstrating both major angiographic features of splenic injury: (a) A.V. shunting (note splenic and portal veins), (b) puddling of contrast due to extravasation of dye.

There are virtually no contraindications to radionuclide scanning. The accuracy of scans is attested to by finding in the literature only one case where the scan was negative and the spleen was found ruptured at operation.[8-10] The incidence of false positives is somewhat higher as splenic injury can be mimicked by pre-existing defect such as infarction or cyst.

Scans are performed by injection of a radionuclide, usually 99 m Tc.-sulfur colloid, around 30 mci./kg. body weight, followed by anterior, left anterior oblique, posterior and left posterior oblique views obtained by means of a gamma camera.[8] Positive findings consist of, (a) blurring of the usual sharp splenic margin or, (b) a filling defect[8] (Fig. 1).

Case 3: A 38-year-old woman tourist, on the day of admission, fell while skiing and subsequently noted persistent left upper quadrant pain. On physical examination, blood pressure was 130/78 and pulse was 88. Bowel sounds were normal. There was no rib tenderness, no mass, and no guarding or rebound noted on abdominal examination. There was, however, some left upper quadrant tenderness. On laboratory examination, hematocrit was 48, white count

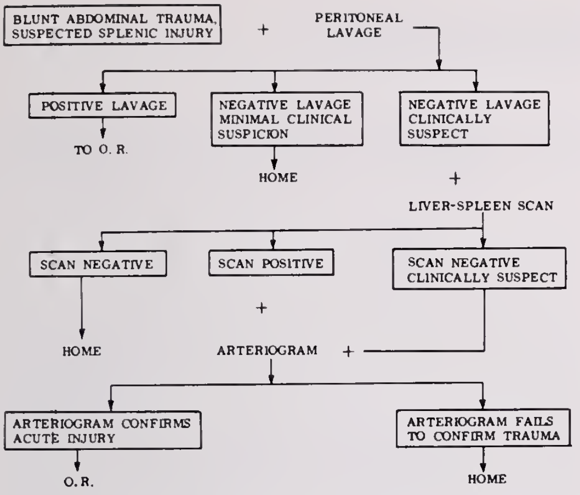
BLUNT ABDOMINAL TRAUMA, SUSPECTED SPLENIC INJURY
+
PERITONEAL LAVAGE
POSITIVE LAVAGE
TO O. R.
NEGATIVE LAVAGE MINIMAL CLINICAL SUSPICION
HOME
NEGATIVE LAVAGE CLINICALLY SUSPECT
+
LIVER-SPLEEN SCAN
SCAN NEGATIVE
HOME
SCAN POSITIVE
+
ARTERIOGRAM
+
SCAN NEGATIVE CLINICALLY SUSPECT
ARTERIOGRAM CONFIRMS ACUTE INJURY
O. R.
ARTERIOGRAM FAILS TO CONFIRM TRAUMA
HOME

Fig. 3. Proposed management of patient with suspected splenic injury.

was 13.4, and urinalysis was normal. A splenic arteriogram was carried out and was normal.

The patient was admitted to the hospital and observed overnight, during which time her vital signs remained unchanged and her hematocrit was stable. She enplaned the same day for California.

COMMENT:

This patient avoided several days observation and hospitalization by virtue of a normal arteriogram done in a hospital which lacked facilities for isotope scans. In retrospect, a normal peritoneal lavage would probably have provided equivalent assurance of the patient's welfare and saved her the price of an arteriogram and a night in the hospital.

Arteriograms

Angiography is the most conclusive diagnostic study of splenic injury as it is highly specific and accurate in over 95 per cent of cases.[11] Because positive scans do not indicate the nature of the abnormality, they should be followed by arteriography. When scanning facilities are not available, arteriograms should be obtained for the same indications as outlined for scans. Contraindications to angiography, performed with the Seldinger technic, are few, and a previous reaction to contrast is the only absolute contraindication. The rate of serious complications is said to be around 0.5 per cent with a mortality rate of 0.3 per cent.[11,12]

Diagnostic angiographic features of splenic rupture are: (a) arterial leakage and (b) arteriovenous shunting. Leakage of contrast is seen in approximately 85 per cent of cases and appears as irregular collections of the contrast confined to the splenic borders with rare extension outside the capsule. Visualization of the splenic vein in less than 2.5 seconds indicates arteriovenous shunting and appears in approximately 40 per cent of cases.[13] Fig. 2 illustrates these features. Areas of absent contrast material, change in arterial pattern, and splenic enlargement are less reliable signs and may lead to a false positive diagnosis.[2] False negative studies are most often the result of examinations performed without selective injection or failure to film in multiple projections.

Summary

Peritoneal lavage, splenic scan, and splenic arteriography can vastly increase the speed and accuracy of patient evaluation when splenic injury is suspected (Fig. 3). Although certain pitfalls exist, their wider use is advocated.

ACKNOWLEDGMENT

Our appreciation is extended to Maralyn Hansen for her assistance in typing and correcting the paper.

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Plethysmographic monitoring*

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A useful non-invasive technic for management of patients with vascular disease.

THE PLETHYSMOGRAPH, INTRODUCED IN 1905 by Brodie and Russell,[1] has become a widely used instrument in monitoring blood flow in man. The mercury strain gauge plethysmograph provides a simple method to evaluate the success of vascular surgery. This instrument furnishes a sensitive and immediate indication of the success of operations by measurement of restored digital pulse volume.

The plethysmograph, being versatile and simple, has several forms. We have used the one using a mercury strain gauge to monitor digital pulses after vascular reconstruction, injection of chemical vasodilators and sympathectomies. The mercury strain gauge plethysmograph, in addition to physical examinations and angiography, aids in the evaluation of the patients with vascular disease. Information obtained by plethysmograph is used to complement, not replace, the data obtained by other methods. The value of this instrument is illustrated in the following case reports.

Methods

The mercury filled strain gauge is made to fit securely around the digit. The output from the plethysmograph is recorded on an ECG machine at the bedside or in the operating room. Measurements taken reflect pulse amplitude and wave form contour. In arterial disease, the ascending (anacrotic) limb of the pulse curve rises slowly, and the dicrotic notch of the slowly descending (catacrotic) limb may be absent. Also, the size of the pulse wave is decreased.

Operative monitoring has been used in vascular reconstruction on 21 patients, to date, as follows: femoral popliteal grafts, 3 patients; axillo-femoral grafts, 3 patients; aorta femoral grafts, 7 patients; aorto-iliac grafts, 5 patients; and aorto-iliac-femoral endarterectomy, 3 patients.

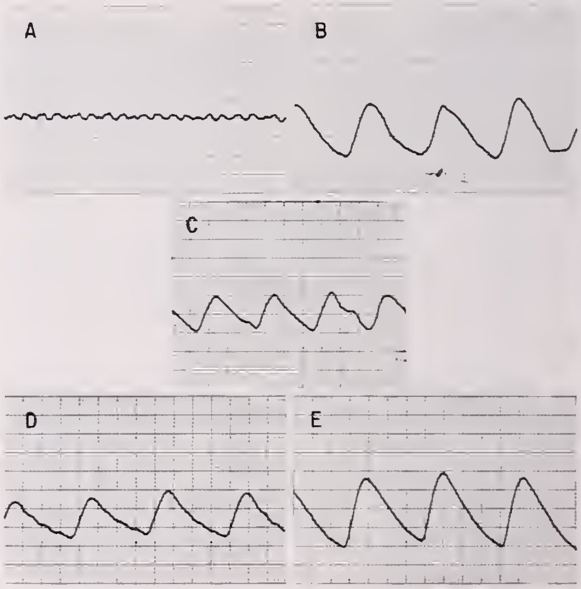

Fig. 1. Plethysmographic tracings of patient with superficial femoral occlusion. A—Right great toe on admission. B—Left great toe on admission. C—Right great toe after vein bypass completed. D—Right great toe 24 hours postoperatively. E—Left great toe 24 hours postoperatively.

CASE REPORTS

Case 1: A 45-year-old white male entered the hospital with chief complaint of pain in his right calf which interfered with his work. He had half-block claudication without rest pain. Physical examination disclosed strong femoral pulses bilaterally with absent popliteal and pedal pulses on the right and strong pulses on the left. The right foot was cooler than the left. Angiogram demonstrated an occlusion of the right superficial femoral artery. Plethysmographic tracing (Fig. 1) showed the decreased digital flow on the right compared to the left. The patient was monitored with the plethysmograph during a femoral popliteal saphenous vein bypass graft. After opening the graft, there was an immediate response of digital flow and a maximum response twenty-four hours following surgery.

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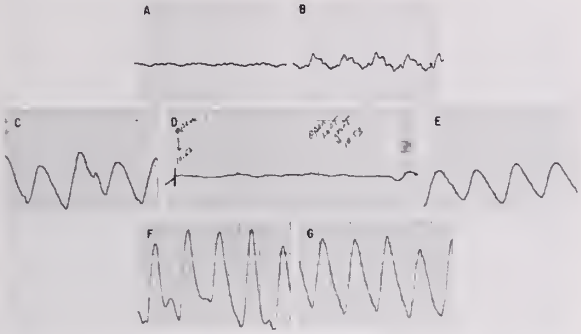

Fig. 2. Plethysmographic tracing of patient with aorto-iliac occlusion. A—Right great toe on admission. B—Left great toe on admission. C—Right great toe after opening dacron bypass graft. D—Left great toe after opening dacron bypass graft. E—Same as D two minutes later. F—Right great toe three weeks postoperatively. G—Left great toe three weeks postoperatively.

Case 2: A 55-year-old man was admitted because of half block claudication, rest pain and numbness of both feet. Physical examination disclosed diminished pulses in both femoral arteries and absent popliteal and pedal pulses. Plethysmographic findings on admission are shown in Fig. 2. Two weeks after a carotid endarterectomy for TIA's, the patient underwent aorto-iliac bypass graft. Plethysmograph monitoring (Fig. 2) showed an immediate pulse response on opening the right side of the graft; the left side had a poor initial response followed by a good response in two minutes. Good digital flow was present on followup three weeks postoperatively.

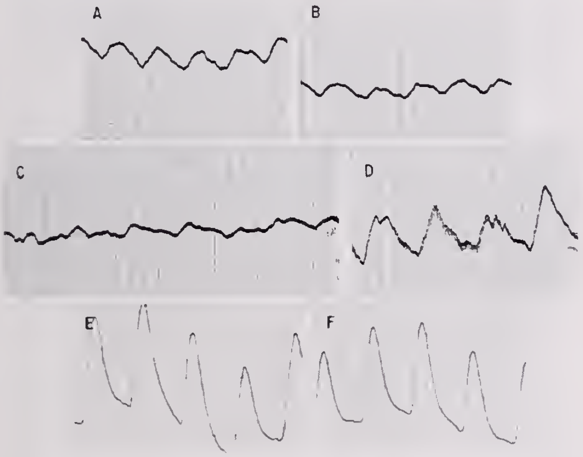

Fig. 3. Plethysmographic tracing of patient with aorto-iliac-femoral occlusive disease. A—Right great toe on admission. B—Left great toe on admission. C—Right great toe after opening dacron bypass graft. D—Left great toe three minutes after opening dacron bypass graft. E and F—Right and left great toes respectively three days postoperatively.

Case 3: A 65-year-old farmer was admitted because of claudication and rest pain. Angiograms demonstrated occlusion of the abdominal aorta with little flow. Plethysmographic tracings showed decreased flow in both feet (Fig. 3). On completion of an aorto-femoral bypass graft, a diminished right pulse was immediately seen after opening the graft; whereas, the left had a three minute delay before a good wave form was present (Fig. 3). Maximum response was seen at three days (Fig. 3).

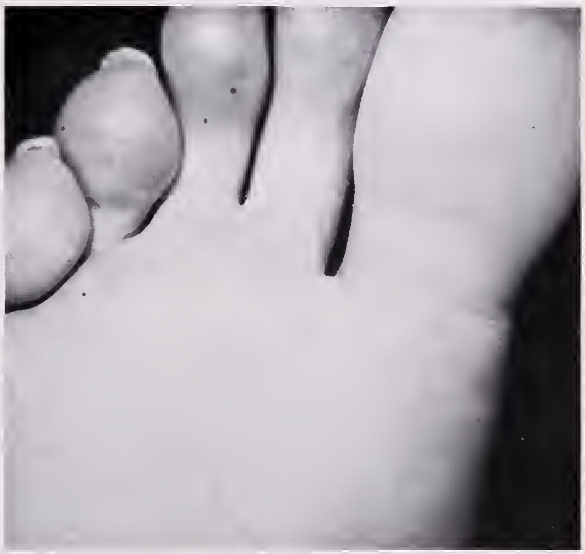

Fig. 4. Cyanosis of toes in patient with vasospastic component to vascular disease.

Case 4: A 53-year-old man was admitted a year following an aorto-femoral Y graft, because of bilateral ankle swelling and painful feet with cyanosis of the right toes (Fig. 4) and coolness of both feet. The femoral pulse was decreased on the right. Pedal pulses were absent bilaterally. Femoral angiogram showed a right popliteal occlusion. The patient was treated with the injection of 1 mg. reserpine in each femoral artery which caused marked improvement in both symptoms and clinical appearance of the right toes. Plethysmography confirmed the clinical impression (Fig. 5), that bloodflow was improved.

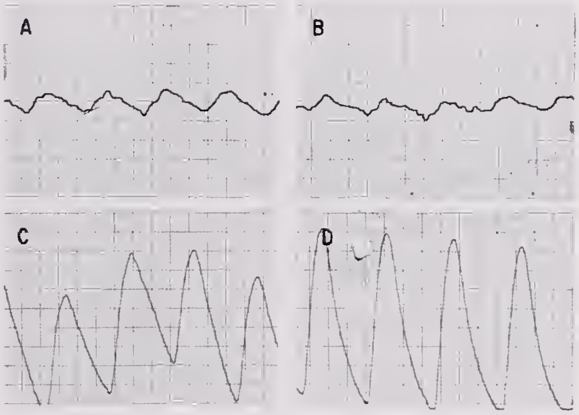

Fig. 5. Plethysmographic tracing of patient with vasospastic component to vascular disease. A and B—Right and left great toes respectively on admission. C and D—Right and left great toes respectively 24 hours after intro-arterial reserpine in each lower extremity.

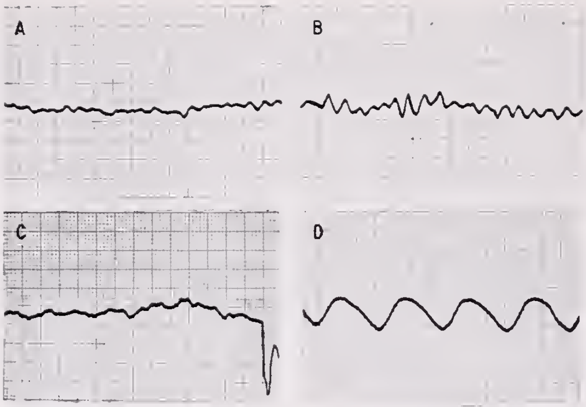

Fig. 6. Plethysmographic tracing of patient with causalgia as residual of frostbite injury. A and B—Right left great toes on admission. C—Right great toe after left lumbar sympathectomy. D—Left great toe 24 hours after left lumbar sympathectomy.

Case 5: A 46-year-old man came to the hospital because of pain in both feet resulting from a previous frostbite injury sustained during the Korean War. The pain was exacerbated by exposure to cold. Physical examination showed decreased pulses in both lower extremities and cyanosis of the toes. Plethysmographic tracing confirmed diminished flow to the toes (Fig. 6). A sympathectomy was performed on the patient's left side, resulting in an increase of blood flow to the affected limb, (Fig. 6). The patient reported the left limb was warm and painfree. The patient was discharged to return at a later date for a right lumbar sympathectomy.

Discussion

These cases illustrate the use of the plethysmograph to follow a patient's course following a vascular procedure. The normal wave pattern consisting of a sharp systolic phase, a sharp peak, a rapid fall and a dicrotic notch is absent in a patient with vascular disease.[2] This non-invasive measurement can be repeated multiple times without danger to the patient. Plethysmography is easy to perform and requires a minimal amount of equipment. We utilize plethysmography as an adjunct to physical examination to follow the post-operative or post-therapeutic course of patients with peripheral vascular disease. Plethysmographic determinations may detect postoperative vascular abnormality before symptoms occur.

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Hematoma of rectus abdominis muscle complicating pregnancy*

A Case Report

S. Steve Yasuzawa, MD and Richard P. Perkins, MD, Denver

SPONTANEOUS RUPTURE of the deep epigastric vasculature and rectus abdominis muscle is a relatively rare event. In the past, reports have been of few cases, primarily associated with trauma in the context of unusual stress or uncommon predisposition. A notable per cent of these have occurred with pregnancy. The case to be presented demonstrates many characteristic features of the process, with a favorable outcome.

CASE REPORT

The patient, a 32 year old white female, gravida three, para two, was referred to the University Medical Center for the possibility of a mass obstructing the pelvic inlet or possible placenta previa. Her last normal menstrual period was February 20, 1973, with an expected date of confinement of November 26, 1973. Her weight gain had been 45½ pounds. She had been followed by her private physician, who first heard fetal heart tones on August 29, 1973 (27 weeks by dates). She was referred at term by her dates, with a history of 18 hours of left lower quadrant pain which developed suddenly after a severe coughing episode. The pain had continued episodically.

The patient complained that for two days prior to the onset of the pain she had had symptoms of an upper respiratory infection with a severe cough. She had not noted chest pain or hemoptysis. She felt that the pain was similar to labor, only localized to the left abdomen. Her last bowel movement was one day prior to admission. She had experienced nausea and vomiting for one day prior to admission. She denied fever or chills, and there was no history of any similar pain in the preceding parts of her pregnancy. She denied sharp or blunt trauma to the abdomen. The fetus had remained active.

The patient was admitted with the diagnosis of possible early labor. There was no history of spontaneous rupture of membranes or vaginal bleeding. The patient's physician had noted that the vertex was not engaged and that the pain was increasing in severity. A flat plate and pelvimetry had been obtained, which confirmed that the vertex was not in the pelvis but in the right iliac fossa. She was admitted for observation.

Past medical history, family, and social histories were non-contributory. Review of systems was unremarkable except for a chronic cigarette cough.

On physical examination, BP was 120/90, temperature was 36.7°C., pulse 128, and respirations 24. She was a well-developed, well-nourished white female, moderately obese, gravid, and in moderate distress secondary to left-sided abdominal pain. The throat was slightly injected. The neck was supple without masses and without adenopathy. The breasts were gravid without masses or tenderness. Chest examination revealed bilateral coarse rhonchi, without dullness or rales. The heart showed a regular rate without murmurs or rubs, but with tachycardia. The abdominal examination showed a 20 x 10 cm. left abdominal mass, questionably separate from the uterus, tender to slight palpation and firm, without overlying skin discoloration. Bowel sounds were normal. The uterine fundus was soft and predominantly non-tender, but the mass could not definitely be separated from it. Fetal parts were easily palpable with the vertex in the right iliac fossa. Fetal heart tones were heard at a rate of 160 beats/min. Estimated fetal weight was 2400 grams. No uterine contractions were palpable. The cervix was 2 cm. dilated, 10 per cent effaced, with the vertex floating on the right side of the pelvis. The bag of waters was palpable and no vaginal bleeding was noted. There was a fullness in the left pelvic area. The remainder of the examination was unremarkable.

Admission blood studies demonstrated a hematocrit of 34% and WBC of 8900 with 81% polymorphonucleocytes and 10% lymphocytes. The platelet count was 505,000. Repeat hematocrits were 37% at 5 hours, 27% at 10 hours, and 26% at 14 hours after admission. Fibrinogen determinations were normal. Blood type was O,Rh positive. Gonorrhea culture was negative. Throat culture disclosed non-specific bacteria. Urine culture was negative. On the preoperative chest x-ray there was an infiltrate in right middle lobe.

By external fetal monitoring there was fetal tachycardia of 170-180 beats/min. with occasional U-shaped decelerations. (Fig. 1) No uterine contractions could be demonstrated. The decelerations responded to oxygen and left-sided positioning of the patient.

The patient was admitted to the Labor Deck. She was observed overnight and serial hematocrits, as recorded above, were obtained. During this time she was continuously monitored externally for fetal heart tones and uterine contractions. Her pain continued to be persistent with episodic severe bouts. By the next morning she was complaining that

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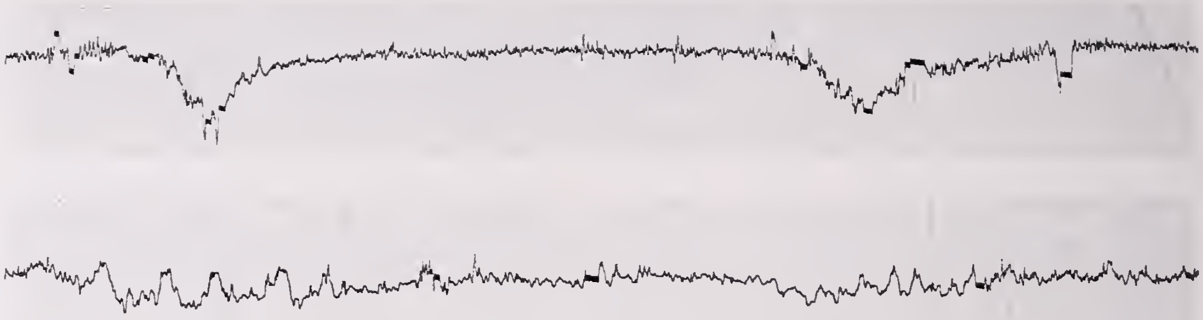

Fig. 1. External fetal heart rate tracings. The upper represents recordings prior to left-sided positioning and oxygen therapy. The lower line of the upper tracing (the tocodynamometry) was flat indicating no uterine activity; this had been checked and was functioning normally. The lower tracing was taken after repositioning the patient and commencing oxygen by mask. Though no tocodynamometric results are shown, there was still no activity. Baseline tachycardia persists throughout.

the pain was more severe in the left upper quadrant of the abdomen. Because of the question of contribution of descending colon to her mass and discomfort, she had been given an enema during the evening of the day of admission with good results, but without relief of her pain. Serial hematocrits revealed a progressive fall over the 14 hours after admission. The monitor demonstrated abnormalities as indicated.

Ultrasound examination of the abdomen the morning after admission showed a "large left adnexal mass" which was thought to represent a broad ligament hematoma or an extra-uterine pregnancy (Figs. 2-4). Because of the continued pain, the lack of definitive diagnosis, progressive fall in peripheral hematocrit and possibility of fetal distress demonstrated by the fetal monitor, patient had an exploratory laparotomy and primary low transverse Cesarean section under general anesthesia. Preoperative attempts at amniocentesis to obtain fluid for observation and maturity studies had been unsuccessful.

Immediately upon entering the anterior rectus sheath, it was evident that the abdominal mass was made up of approximately 600 ml. of blood in the left rectus sheath. It was necessary to evacuate most of the hematoma before proceeding with Cesarean section. A 2320 gm. male infant with an Apgar score of 6 at 1 min., and 8 at 5 min., was delivered through a low transverse uterine incision. The amniotic fluid was grossly stained with dark meconium. Placentation was unremarkable.

The uterine incision was closed in the usual manner and attention was then returned to the left rectus sheath hematoma, which had dissected caudally into the left paravesical space, dorsally to the left paravertebral area, and cephalically to the left costal margin. The clots were evacuated and the cavity examined for active bleeding sites. None was identified. The hematoma cavity was irrigated and drained with three 1-inch Penrose drains. The abdominal incision was closed with the aid of retention sutures. The patient received three units of blood. She was placed on penicillin and kanamycin postoperatively. A postoperative chest x-ray showed bilateral pneumonia. A bronchial aspirate obtained for culture at the time of operation grew out many bacteria including *D. pneumoniae.*

In addition to the pneumonia, the patient's postoperative course was complicated by paralytic ileus. The pneumonia cleared with vigorous pulmonary therapy and antibiotic treatment. The chest x-ray was clear on discharge. The ileus responded to nasogastric suction and intravenous fluid administration.

She progressively improved and was fully ambulatory by the fourth hospital day. Her hematocrit was 33% on the third postoperative day and the Penrose drains were progressively advanced after the initial blood discharge slowed. These were removed on the sixth postoperative day. The patient was discharged on the ninth postoperative day with a moderate amount of non-tender induration in the left flank area. Oral iron tablets, tetracycline for a full seven days, was prescribed. She returned one week after discharge for follow up examination and removal of retention sutures. Follow up visit showed the patient to be doing well and free of complaints, with a rising of hematocrit and some resolution of the left flank induration. The patient returned to her private physician for further follow up care. The baby's neonatal course was uncomplicated.

Discussion

In 1937, Brodel and Cullen,[1] in companion articles, presented an elegant treatment of the subject of rectus muscle anatomy and diseases. Subsequent case reports have acknowledged their contributions consistently and have served merely to add new examples of the problems to which they referred.

The importance of making the correct diagnosis and pursuing the correct therapeutic program is illustrated by the data from the pretransfusion era, when moderate maternal (10-15 per cent) and high fetal death rates (25-50 per cent) were noted.[2,3] Interestingly, this entity has received little attention recently, perhaps indicating improved methods of diagnosis and of management.

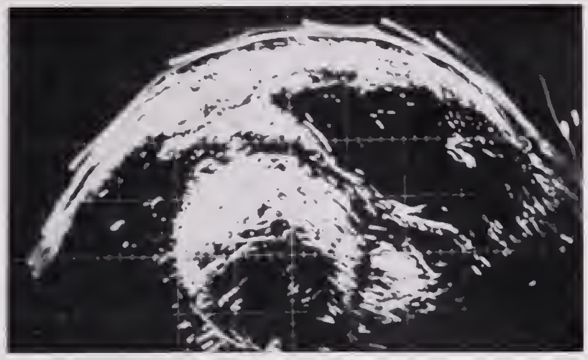

Fig. 2. Ultrasound cross-sectional scan (B-mode) 10 cm. above the symphysis. Fetal parts are seen displaced to the right by a large cystic mass, left anterolateral. A "membrane" is seen between the mass and the fetus.

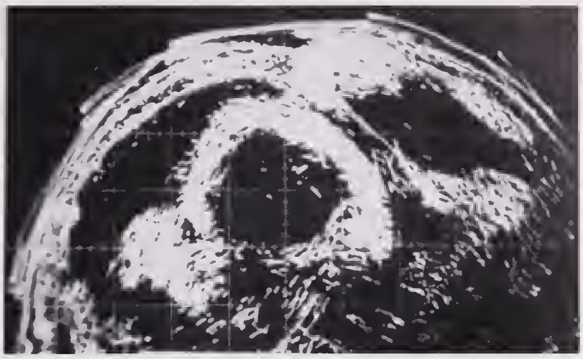

Fig. 3. Same technic as in Fig. 2, 6 cm. further cephalad. Similar findings, indicating the extent of the process. The exact nature and location of the mass in relation to the uterine cavity remains obscure.

In more recent reports, Schafer,[4] and Lucas and Baker[5] have noted an interesting predominance of pregnant patients among those affected with the disease, as compared with the general population. In Schafer's report, 46 per cent of all patients were gravid. He summarized the past experience showing five maternal and twelve fetal deaths in 46 pregnancies. In seventy per cent, the hematoma arose after trivial trauma, usually tussic. Six developed with the strain of labor, and two after a fall. The right rectus was usually involved and four-fifths were localized to the lower half. Lucas and Baker pointed out that since Torpin's report,[3] only one maternal and one fetal death had occurred. Teske[2] had previously outlined 100 cases, most of which had been reported previously, and showed a preponderance of females and debilitated, elderly persons. He also found that over 75 per cent had the pathology confined to the lower abdomen with the right side involved over twice as often as the left.

Herzan[6] was able to find around 500 cases in the literature as of 1967, and outlined the roentgenologic aspects of diagnosis, showing the benefits of cross-table lateral films in delineating the mass.

The exact causes of fetal demise in the absence of maternal death in this process have not been elucidated well. It was of interest to us that despite the maintenance of normal maternal vital signs in our case, suggestive evidence of fetal distress was indicated by typical "late deceleration" dips on external fetal heart rate monitoring and the presence of meconium at Cesarean section. Though there were no contractions recorded to which the decelerations could be related, this may have been explained by insulation of the external pressure transducer from the uterine fundus by the mass. The decelerations had a characteristic wave form and did respond to left-sided maternal positioning and oxygen administration. The presence of the baseline fetal tachycardia rendered the deceleration observations even more worrisome.

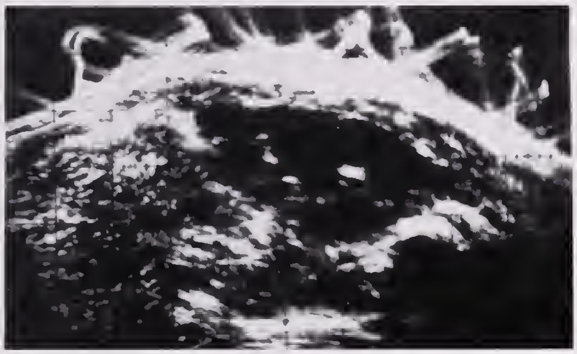

Fig. 4. Longitudinal scan 4 cm. to the left of the midline. The patient's head would be to the left, the symphysis pubis to the right. Note that the cystic mass extends at least the length of the uterus, but still cannot easily be separated from it.

Predispositions noted in this patient were typical. She was pregnant, and for the third time, and did have a troublesome upper and lower respiratory infection with moderately severe cough. Her pain clearly began with a violent tussic episode. There was no clearcut peritoneal irritation, nor pelvic mass palpable, though a "fullness" was noted. Cross-table lateral films would likely have elucidated the nature of the process, but since the correct diagnosis was not strongly suspected, these were not performed.

The ultrasound study was helpful only in retrospect. It can be seen (Fig. 2-4) that a membrane was defined on the medial side of the mass, but at initial reading it was not clear as to whether this represented parietal peritoneum from the abdominal wall (as it was), a leaf of broad ligament, or the chorioamnion pushed away from the uterine wall by a hematoma originating from abruptio placentae. It was the last diagnosis, in light of the apparent fetal distress and falling hematocrit, possible uterine tenderness, and despite the failure of clotting factors to diminish, that led to the ultimate course of action. Apparently, the correct plan was followed with the wrong diagnosis.

Management of such cases has in the past been carried out in some instances without surgical intervention and without adverse outcome. So might it have been in this case, as bleeding appeared to have ceased on exploration, and no definite bleeding point on the peritoneal surface of the rectus was identified. The patient responded well to evacuation of residual clot and drainage of the large cavity. The extent of the clot was unusual by comparison with previous reports, in which the majority were right-sided and the vast majority confined below the umbilicus. In this case the process extended the entire length of the left rectus abdominis and from beneath the costal margin to beneath the symphysis pubis. It is likely that the blood loss was greater than that retrieved at surgery.

As many authors have suggested, the key to the diagnosis is to suspect the diagnosis. X-ray studies and/or ultrasound evaluations can aid if well executed and interpreted. There is no obvious reason for a normotensive mother to have fetal distress in this condition, but we feel that our patient did and that therapy was appropriate. Conceivably, more conservative management could be contemplated in earlier gestations, with reasonably good outcome anticipated in almost every case. Normal external fetal heart rate monitor tracing could make the proponent of conservative, non-surgical management considerably more at ease.

Summary

A case of spontaneous rectus abdominis muscle hematoma of substantial extent is presented, with good fetal and maternal outcome. The etiology and pathogenesis of this rare complication of pregnancy are discussed, and attention directed to the seriousness of the disorder, particularly in the past. The difficulties of diagnosis are explained.

ACKNOWLEDGMENT

The authors wish to thank Malcolm J. Dickerson, M.D., of Brush, Colorado, for permission to publish this report on his patient.

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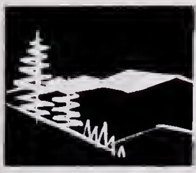

COLORADO

Hand Surgery Specialists to Organize

Establishment of the Rocky Mountain Hand Surgery Society among board certified or qualified general orthopedic and plastic surgeons with the aim of sharing knowledge, exchanging ideas, and supporting advancement of the practice and investigation of hand surgery is currently in process.

Officers are Robert Horner, MD, President; Donald Ferlic, MD, Vice President; Barbara Parks, MD, Secretary-Treasurer; William Powers, MD, Program Chairman; Richard Kem, MD, and Richard Thompson, Councilmen at Large.

Inquiries should be directed to Barbara Parks, MD, 1666 South University Blvd., Denver, Colorado 80210.

Kozloff Elected Fellow of AAAS

Lloyd Kozloff, MD, professor and chairman, Department of Microbiology, University of Colorado School of Medicine, recently was elected a fellow of the American Association for the Advancement of Science and as chairman of the Virology Division, American Society for Microbiology. An author or coauthor of more than 40 articles, Doctor Kozloff has been a major contributor to and founder of biochemical virology. He received his Ph.D. degree in biochemistry from the University of Chicago.

In addition to ASM, the 51-year-old biochemist is a member of the Society of General Physiology, American Chemical Society and the American Society of Biological Chemists. He has been editor of the *Journal of Virology* and on the editorial board of the *Journal of Bacteriology.*

WYOMING

Gillette Hospital Joins ECG Computer Network

Patients treated at Campbell County Memorial Hospital, Gillette, Wyo., for possible heart problems now have the added benefit of a computer's opinion about their cardiac activity.

Under a project sponsored by the Denver-based Colorado-Wyoming Regional Medical Program (CWRMP), the 31-bed hospital has been linked to the Community Electrocardiographic Interpretative Service (CEIS) in Denver, more than 400 miles away. The system became operational in November.

Electrocardiograms (ECGs—recordings of the electrical actions of the heart) will be transmitted from the Gillette hospital over long-distance telephone lines to the CEIS computer in Denver. Within about five minutes a complete computer analysis of the ECG is transmitted back to the hospital via teletype for consideration by local physicians.

The computer system is the only one of its kind in the Rocky Mountain area and is one of few such systems in the country. Campbell County Memorial is the eighth Wyoming hospital to join the computer network and the sixth to receive CWRMP assistance in obtaining the service.

CEIS, a non-profit service corporation, has been in operation in Denver since late 1969 under the direction of Dr. Robert V. Elliott, a cardiologist. Thirty hospitals, including several in Kansas and Nebraska, are currently part of the CEIS network.

MEDICAL SCHOOL NOTES

University of New Mexico Chemotherapy Grant

A new cancer grant, designed to provide the most current diagnostic and therapeutic care to residents throughout New Mexico, has been made to John H. Saiki, M.D., associate professor of medicine at the University of New Mexico School of Medicine. The grant from the National Cancer Institute totals $227,641 over a three year period. Dr. Saiki is in charge of the medical oncology clinic at the Cancer Research and Treatment Center.

The grant will allow the doctors to treat cancer patients with the most current effective investigational drugs and those drugs which already are proven and accepted, either alone or in combination with radiotherapy. Treatments will follow detailed procedures established by members of the Southwest Cancer Chemotherapy Study Group, composed of 27 major medical centers throughout the United States.

Co-investigators will be D. C. Pinkerton, MD, of Lovelace Clinic pediatric department; W. R. Hardy, MD, professor of medicine at UNM and chief of hematology section at Veterans Administration (VA) Hospital; B. M. Wimer, MD, chief of the Lovelace Clinic department of hematology; J. A. Antoine, MD, of the Lovelace hematology-oncology division; J. H. Saiers, MD, hematology-oncology, UNM; M. M. Kligerman, MD, director, Cancer Research and Treatment Center, UNM; C. J. Sternhagen, MD, radiotherapist, UNM; D. L. Simmons, MD, chief of radiotherapy, St. Joseph Hospital; M. H. Duncan, MD, hematology-oncology, UNM; Stanley Stark, MD, pediatrics, UNM.

"Studying patients in these groups permits us to evaluate clinical investigations within a shorter span of time," Dr. Saiki said. "Having a surgeon, pathologist, radiotherapist, immunologist, and chemotherapist on the research team gives us a unique opportunity for looking at many new approaches to cancer patient care."

The grant was announced in Washington January 14, 1975, by Congressman Manuel Lujan (R-NM). First year funds are for $72,306; second year $75,810; and third year $79,525.

THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Centennial Bibliography of Huntington's Chorea 1872-1972: Bruyn, G. W., Baro, F., and Myrianthopoulos, N. C. Leuven University Press, 1974. 314 p. Gift.

Clinical Pediatric Oncology: Sutow, Wataru W., ed. Mosby, 1973. 602 p. $37.50. (Gift of American Cancer Society)

Clinical Hypertension: Kaplan, Norman M. Medcom, 1973. 347 p. $30.00.

Depression in Medical Practice: Enelow, Allen J. Merck, Sharp and Dohme, 1970. 222 p. Gift—St. Luke's.

The Esophagus: Payne, William S. Lea and Febiger, 1974. 339 p. $16.00.

Hodgkin's Disease: Smithers, David, ed. Churchill Livingstone, 1973. 258 p. $30.00. (Gift of American Cancer Society)

Immediate Hypersensitivity, The Molecular Basis of the Allergic Response: Stanworth, D. R. American Elsevier Publishing Co., 1973. (**Frontiers of Biology,** v. 28) $27.00.

Lid Surgery—Current Concepts: Sidney A. Fox. Grune and Stratton, 1972. 170 p. $16.75.

Life's Road and Other Poems: Mumey, Nolie, Range Press, 1974. Gift.

Medical and Healthcare Stock Market Guide: Hale, Adeline B. and Hale, Arthur B., ed. International Bio-Medical Information Service, Inc., 1972. 300 p. Gift.

Muscle Biopsy: A Modern Approach: Dubowitz, Victor, Brooke, Michael H., and Neville, Hans E. Saunders, 1973. (**Major Problems in Neurology,** v. 2).

Overview of Blood: Bishop, Charles, ed. Blood Information Service, 1974. $8.00.

Paying the Doctor, Systems of Remuneration and Their Effects: Glasser, William A. Johns Hopkins Press, 1970. 323 p.

The Peripheral Nervous System: Hubbard, John. Plenum Press, 1974. $32.50.

Psychiatry and Law: Slovenko, Ralph. Little, Brown and Co., 1973. 726 p. $28.50.

Psychosomatic Concepts: Grinker, Ray R. Jason Aronson, 1973. 219 p. $10.00.

Psychosomatic Medicine: Munro, Alistair, ed. Churchill Livingstone, 1973. 95 p. $6.00.

Radiation Oncology; Rationale, Technique, Results: Moss, William T. 4th ed. Mosby, 1973. 622 p. $30.00. (Gift of American Cancer Society)

Referring the Psychiatric Patient, A Guide for the Physician: Kimsey, Larry R., and Roberts, Jean L. Thomas, 1973. 80 p. (**American Lectures in Clinical Psychiatry,** no. 878) Review Copy.

Symposium on Vascular Disorders and Hearing Defects: Johns Hopkins Medical Institutions. University Park Press, 1973. 357 p. $17.50.

Book Review

Regulating New Drugs: Richard L. Landau, Editor, The University of Chicago Center for Policy Study, 1973, Forty-two Conference Participants, 297 p., paper-back $5.25.

The widespread disillusionment and criticism relating to the Federal Drug Administration has led to this detailed and learned appraisal of the FDA. Professors of Biology, Economics, Law, Pharmacology, Political Science, Medicine, Psychiatry, Radiology, and Surgery in conjunction with Sociologists, Drug Manufacturers, and Federal Officials, have produced this most detailed criticism of the FDA. Economist Sam Peltzman, whose intricate presentation occupies 99 pages, one-third of the book, concludes "If the Food, Drug and Cosmetics Act was intended to benefit consumers, the inescapable conclusion to which this study points is that the intent is better served by reversion to the status quo ante 1962." (page 207, last paragraph)

Certainly the most engaging and perhaps the most productive presentation for the benefit of the USA is Sir Derrick Dunlop's *The British System of Drug Regulation,* page 230 ff. We still have much to learn about government of, by, and for the people. It appears that George the Third's current government has done rather better than we have. See the article and full page advertisement concerning the use of anti-androgens in the *Brit. J. Psychiatry* 125:310-5, September 1974. This reviewer has long considered the Swiss to be perhaps the most civilized nation on this tortured globe, and hence he finds the contribution by Hubert Bloch worthy of close consideration, along with Sir Derrick's.

It is now apparent that the FDA took far more credit in the thalidomide affair than was its due. "The facts are that thalidomide had been blocked for non-relevant reasons, and was actually moving toward approval when the drug company itself reported the terrible news" (page 27, line 1). Procrastination appears to be the FDA's major skill.

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OBITUARIES

Robert J. Ansley, MD, Wesminster, Colorado, died Friday, January 17, 1975 at St. Anthony's Hospital, Denver, following a massive heart attack. Born February 24, 1922 in Chicago, Illinois, he was educated in the public schools of that city. He attended Elmhurst College then later the University of Illinois, from which institution he received a bachelor of science degree. He received his MD from the medical school of the University of Illinois in Chicago in 1953. After an internship at St. Luke's Hospital, Denver, he opened an office for the general practice of medicine in Westminster. Later he went into a partnership with Drs. Robert Murch and John Ford, and built the Bradburn Medical Building, Westminster.

Doctor Ansley served with the United States Army in the South Pacific during World War II, and was a recipient of the Purple Heart Award.

He was a member of the Clear Creek Valley Medical Society, the Colorado Medical Society, and the American Medical Association. For the Clear Creek Valley society Doctor Ansley served as Chairman of the North Unit, and also served in a wide variety of positions including Delegate and Alternate Delegate.

He was twice a widower. He was married to Frances Hansen of Boulder on January 12, 1974. Surviving besides his widow are a daughter Barbara of Denver and five sons, Randall of Los Angeles, Mark of Denver, and Robert, James, Jonathan, and pher, all of Arvada. A sister, Mrs. Gertrude Gray of New Lisbon, Wisconsin, and three brothers, Dr. Elmer F. of New York City, Leonard of Chagrin Falls, Ohio, and Jerome of Mt. Prospect, Illinois also survive the doctor.

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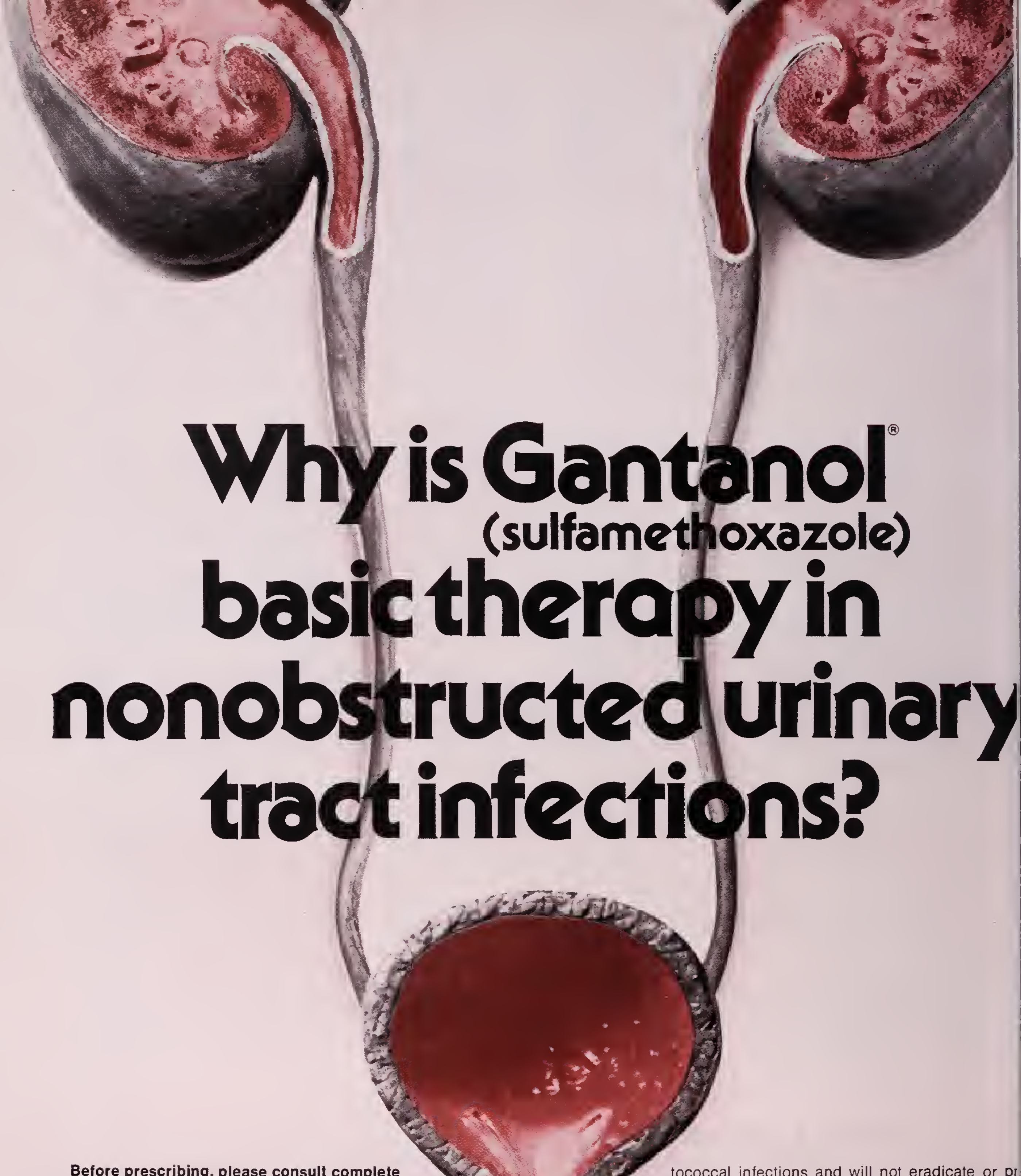

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a, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous*
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Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria and paralytic ileus.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils, tachycardia and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. Use a narcotic antagonist in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: *Tablets,* 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. *Liquid,* 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

454 R

MEETINGS

American Medical Association
American Bar Association

1975 NATIONAL MEDICOLEGAL SYMPOSIUM

MGM Grand Hotel, Las Vegas, Nevada

March 14-16, 1975

Contact: MGM Grand Hotel, Convention Reservations, P.O. Box 11087, Las Vegas, Nevada 89111.

American Urological Association, Allied

BI-ANNUAL SEMINAR

Craig Rehabilitation Hospital Conference Room, 3425 S. Clarkson St., Englewood, Colorado.

March 15, 1975

Contact: Donna Hoffman, Colorado Urological Center, PC, 1245 E. Colfax Avenue, Denver, Colorado 80218.

Colorado Association for Continuing Medical Laboratory Education

SEMINARS IN ANATOMIC PATHOLOGY

CACMLE Center, Mercy School of Nursing Building, 16th at Milwaukee Streets, Denver

March 20-22, 1975

Contact: CACMLE, Inc., Box 84, Mercy School of Nursing Building, 1601 Milwaukee St., Denver, Colorado 80206.

University of Colorado Medical Center

HEALTH HAZARDS IN THE WORKING ENVIRONMENT

University of Colorado School of Medicine

March 21-22, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 E. 9th Avenue, Denver, Colorado 80220.

* * * * *

CLINICAL ECHOCARDIOGRAPHY SEMINAR

Vail, Colorado

April 2-4, 1975

this way *to a Sun Break*

American College of Physicians

RECENT ADVANCES IN THE IMMUNOPROPHYLAXIS AND CHEMOTHERAPY OF INFECTIOUS DISEASES
Arizona Medical Center Auditorium,
Tucson, Arizona

April 3-5, 1975

Contact: Registrar, Postgraduate Courses, ACP, 4200 Pine St., Philadelphia, Pa. 19104.

Nevada Cancer Control Institute
Las Vegas, Nevada

April 10-11, 1975

Contact: Ms. Irene S. Peacock, 1800 W. Charleston Blvd., Las Vegas, Nevada 89102.

Montana Radiologic Society

ANNUAL BUSINESS MEETING
St. Peter's Hospital, Helena, Montana

April 12, 1975 at 1:30 p.m.

Contact: V. Paul Johnson, MD, 1222 North 27th St., Billings, Montana 59101.

Montana Medical Association

28TH INTERIM MEETING
Colonial Hilton, Helena, Montana

April 11-12, 1975

UCLA Center for Health Sciences

PHYSICIAN EDUCATION PROGRAM IN FAMILY PLANNING
University of California, Los Angeles

April 21-25, 1975

Contact: Irvin M. Cushner, MD, Ob/Gyn Department UCLA Center for Health Sciences, Los Angeles, California 90024.

Instrument Society of America

1975 SPRING JOINT CONFERENCE
Queen Elizabeth Hotel, Montreal, Canada

April 24-27, 1975

Contact: Robert Hand, Instrument Society of America, 400 Stanwix St., Pittsburgh, Pennsylvania 15222.

Stanford University School of Medicine

MANAGEMENT OF THE SURGICAL PATIENT
Mauna Kea Beach Hotel, Kamuela, Hawaii

April 26-May 3, 1975

Contact: Office of Postgraduate Medical Education, Stanford University, School of Medicine, Stanford, California 94305.

American Cancer Society-National Cancer Institute

NATIONAL CONFERENCE ON ADVANCES IN CANCER MANAGEMENT
PART II: DETECTION AND DIAGNOSIS
The Denver Hilton, Denver, Colorado

May 1-3, 1975

Contact: American Cancer Society, 219 E. 42nd St., New York City, NY 10017.

Biennial Western Conference on Anesthesiology

14TH BIENNIAL WESTERN CONFERENCE ON ANESTHESIOLOGY
Princess Kaiulani Hotel, Honolulu, Hawaii

May 4-8, 1975

* * * * *

WORKSHOP
Sheraton Maui Hotel, Island of Maui, Hawaii

May 9-11, 1975

Contact: Murray G. Atnikov, MD, Biennial Western Conference on Anesthesiology, 2574 W. 33rd Ave., Vancouver 13, British Columbia, Canada.

Cardiovascular Department Sunrise Hospital

CURRENT CONCEPTS IN CARDIOLOGY
Caesar's Palace, Las Vegas, Nevada

May 5-8, 1975

Contact: American Heart Association, 44 East 23rd St., New York City, New York 10010.

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    * Complete medical library, with periodicals, recordings, and audio-visual aids.
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SOCIETY OFFICERS

Colorado Medical Society

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Session of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: Howard T. Robertson, Denver.

President-elect: Joseph S. Pollard, Jr., Colorado Springs.

Vice President: Harlan B. Huskey, Fruita.

Treasurer: Otis J. King, Jr., Colorado Springs.

Constitutional Secretary: Stanley J. Sontag, Lakewood.

Delegates to the A.M.A.: John M. Wood, Englewood, Dec. 31, 1975; Robert E. McCurdy, Denver, Dec. 31, 1975; Kenneth A. Platt, Westminster, Jan. 1, 1975-Dec. 31, 1976.

Alternate Delegates to the A.M.A.: Clyde E. Stanfield, Denver, Dec. 31, 1976; William Y. Takahashi, Boulder, Dec. 31, 1975; Joseph L. Kovarik, Dec. 31, 1975. One position to be filled.

Speaker, House of Delegates: Robert A. O'Dell, Aurora.

Vice Speaker, House of Delegates: R. Jack Warren, Denver.

Foundation Advocate: H. Sol Cersonsky, Denver.

Scientific Editor for Colorado and Chairman of the Editorial Board, Rocky Mountain Medical Journal: Carl H. McLauthlin, Denver.

Scientific Editor Emeritus, Rocky Mountain Medical Journal: Douglas Macomber, Denver.

Executive Director: Mr. Donald G. Derry, 1601 East 19th Avenue, Denver, Colorado 80218. Telephone (303) 534-8580.

New Mexico Medical Society

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Session in the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Session.

President: U. G. Hodgin, Jr., Albuquerque.

President-elect: Robert Cutler, Espanola.

Vice President: Walter Hopkins, Lovington.

Secretary-Treasurer: Ronald V. Dorn, Jr., Albuquerque.

Immediate Past President: Armin T. Keil, Raton.

Speaker, House of Delegates: William J. Hossley, Deming.

Vice Speaker, House of Delegates: John D. Abrums, Albuquerque.

Delegate to A.M.A.: Emmit M. Jennings, Roswell.

Alternate Delegate to A.M.A.: Armin T. Keil, Raton.

Councilors for Three Years: George P. Bunch, Las Vegas; Robert Zone, Santa Fe; Livingston Parsons, Albuquerque; John Moore, Roswell.

Councilors for Two Years: James Loucks, Los Alamos; William C. Gorman, Albuquerque; Donald Wolfel, Albuquerque; James Gaba, Artesia; Jerome P. Pucelik, Las Cruces; Theodore Draelos, Silver City; Donald Draney, Alamogordo.

Councilors for One Year: Edgar Smith, Albuquerque; John G. Griffin, Albuquerque; Samuel Neff, Clovis; T. G. McCormick, Hobbs; Norton Ritter, Gallup; Jack Coats, Farmington.

Scientific Editor for New Mexico Rocky Mountain Medical Journal: Marcus J. Smith, Santa Fe.

Assistant Scientific Editor for New Mexico, Rocky Mountain Medical Journal: John H. Saiki, Albuquerque.

Associate Editor for New Mexico, Rocky Mountain Medical Journal: Mr. Ralph R. Marshall, Albuquerque.

Executive Director: Mr. Ralph R. Marshall, 3010 Monte Vista Blvd., NE, Albuquerque, 87106. Telephone (505) 265-8494.

Associate Executive Director: Rick Beitler, Albuquerque.

Montana Medical Association

OFFICERS—1974-75—Terms of Officers and Committeemen expire at the Annual Meeting of the year indicated. Where no year is indicated the term is for one year only and expires at the 1975 Annual Meeting.

President: John R. Halseth, Great Falls.

President-elect: David Gregory, Glasgow.

Vice President: Colvin H. Agnew, Billings.

Secretary-Treasurer: Robert P. Yost, Missoula.

Assistant-Secretary-Treasurer: James E. Elliott, Havre.

Delegate to the A.M.A.: Herbert T. Caraway, Billings.

Alternate Delegate to the A.M.A.: Mark B. Listerud, Wolf Point.

Executive Committee: John R. Halseth, Great Falls; David Gregory, Glasgow; Colvin H. Agnew, Billings; Robert P. Yost, Missoula; James E. Elliott, Havre; Herbert T. Caraway, Billings; Mark B. Listerud, Wolf Point; John R. Burgess, Jr., Helena; James K. Cope, Forsyth.

Scientific Editor for Montana, Rocky Mountain Medical Journal: Gerald A. Diettert, Missoula.

Associate Editor, Rocky Mountain Medical Journal: Mr. G. Brian Zins, Helena.

Executive Director: Mr. G. Brian Zins, 2021 11th Avenue, Suite 12, Helena, Montana 59601, Telephone (406) 443-4000.

Nevada State Medical Association

OFFICERS—Terms of Officers and Committeemen expire in April 1976.

President: William K. Stephan, Las Vegas.

President-elect: John W. Callister, Reno.

Secretary-Treasurer: John L. Holmes, Las Vegas.

Immediate Past President: Thomas K. Hood, Elko.

Delegate to A.M.A.: Norman Christensen, East Ely.

Alternate Delegate to A.M.A.: Richard C. Inskip, Reno.

Scientific Editor for Nevada, Rocky Mountain Medical Journal: Thomas J. Scully, Reno.

Assistant Scientific Editor for Nevada, Rocky Mountain Medical Journal: Robert W. Williams, Las Vegas.

Associate Editor, Rocky Mountain Medical Journal: Mr. Richard G. Pugh, Reno.

Executive Director: Mr. Richard G. Pugh, 3660 Baker Lane, Reno 89502. Telephone (702) 825-6788.

Wyoming State Medical Society

OFFICERS—1975—Terms of Officers and Committeemen expire December 31, 1975. Terms of office (with the exception of Delegate and Alternate Delegate to A.M.A.) expire at the end of the calendar year rather than at the Annual Session.

President: Donald B. Hunton, Cheyenne.

President-elect: Patrick D. Nolan, Buffalo.

Vice President: James E. Stoetzel, Pine Bluffs.

Secretary: Kent T. Christensen, Casper.

Treasurer: James R. Alexander, Torrington.

Delegate to A.M.A.: Fenworth M. Downing, Sheridan.

Alternate Delegate to A.M.A.: John J. Corbett, Casper.

Speaker of the House: Theodore L. Johnston, Cheyenne.

Vice Speaker of the House: Ross J. Collie, Lander.

Immediate Past President: Paul R. Yedinak, Rock Springs.

Scientific Editor for Wyoming, Rocky Mountain Medical Journal: Francis A. Barrett, Cheyenne.

Associate Editor for Wyoming, Rocky Mountain Medical Journal: Mr. Robert Smith, Cheyenne.

Executive Director: Mr. Robert Smith, P. O. Drawer 4009, Cheyenne, Wyoming 82001. Telephone (307) 635-2424.

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FAMILY PHYSICIAN OR INTERNIST, semi-retired or part-time, for Lake Tahoe, Incline Village, Nevada. Contact: Harry W. Weigel, MD, P.O. Box 3189, Incline Village, Nevada 89450, or call (702) 831-0420. 375-3-1

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Rondomycin®
(methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.
WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**
Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)
Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy
Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)
All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.
Tetracyclines are present in milk of lactating women taking tetracyclines.
To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN. While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.
Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema
PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.
In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.
Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).
Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin
ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.
Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).
Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).
Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.
Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued.
Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia.
Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur.
USUAL DOSAGE: Adults – 600 mg daily, divided into two or four equally spaced doses. More severe infections, an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea: In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule. 900 mg initially, followed by 300 mg q.i.d. for a total of 5.4 grams.
For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended.
Eaton Agent pneumonia 900 mg daily for six days
Children – 3 to 6 mg/lb/day divided into two to four equally spaced doses.
Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided.
Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere. Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding.
In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses.
In streptococcal infections, a therapeutic dose should be given for at least 10 days.
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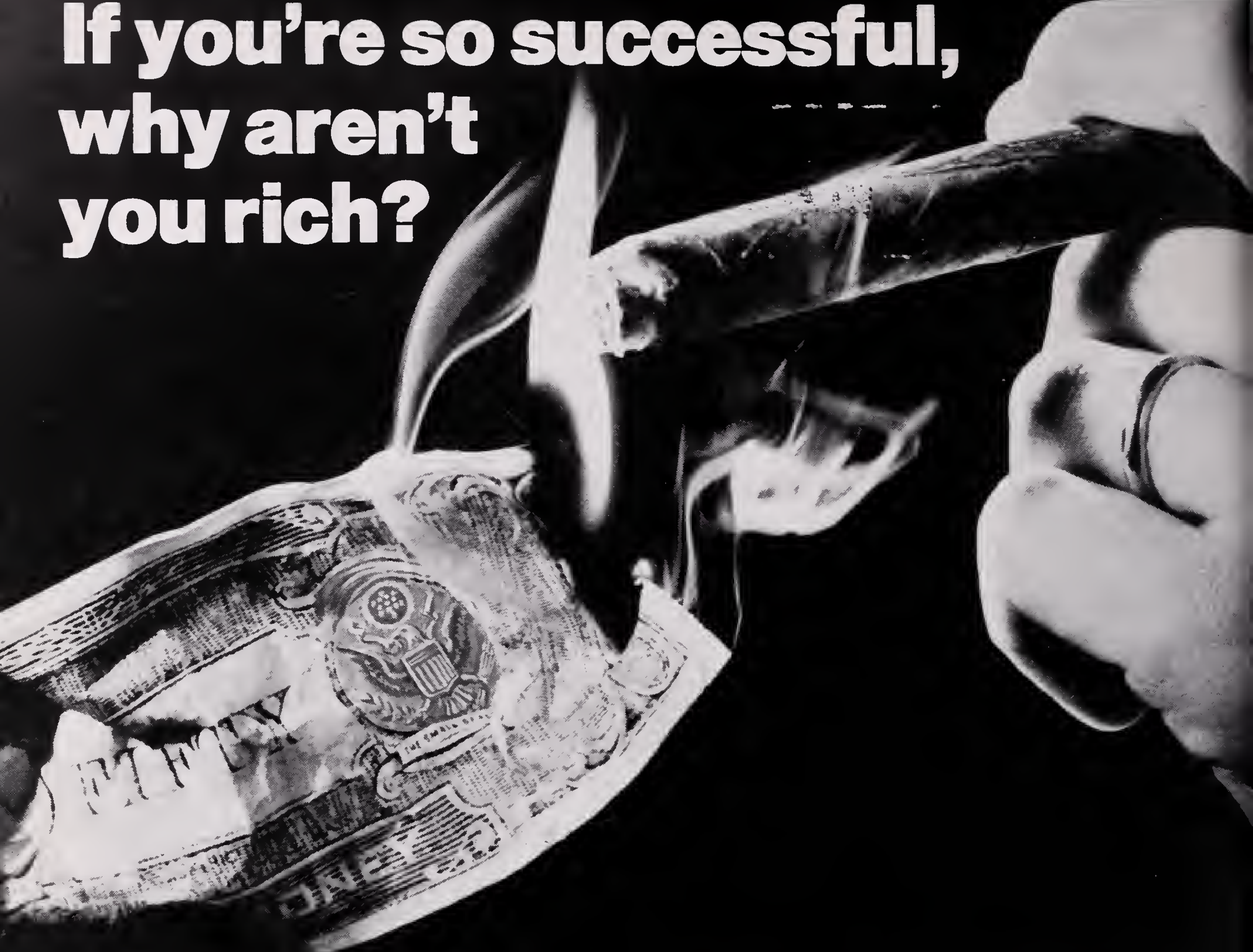

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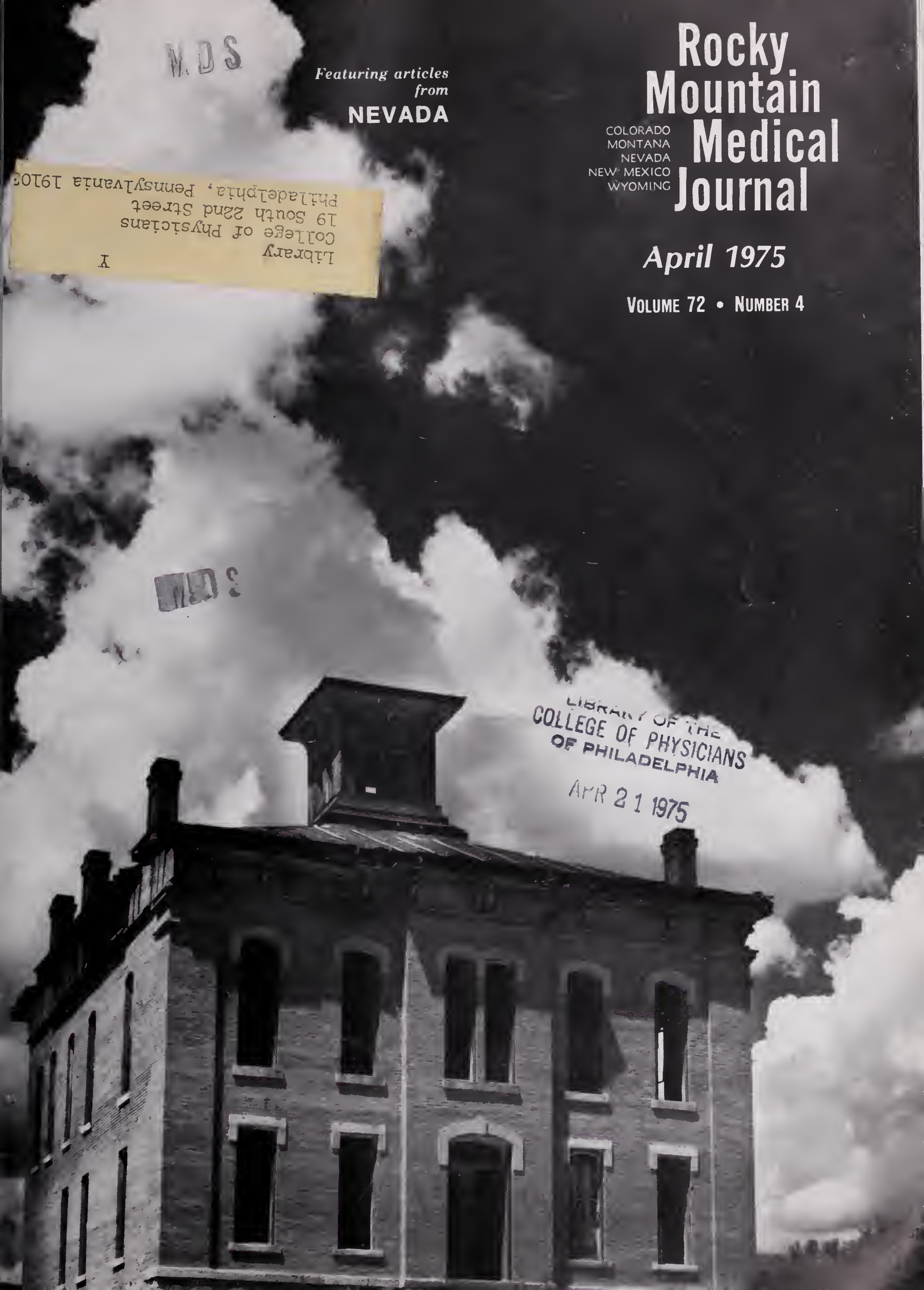

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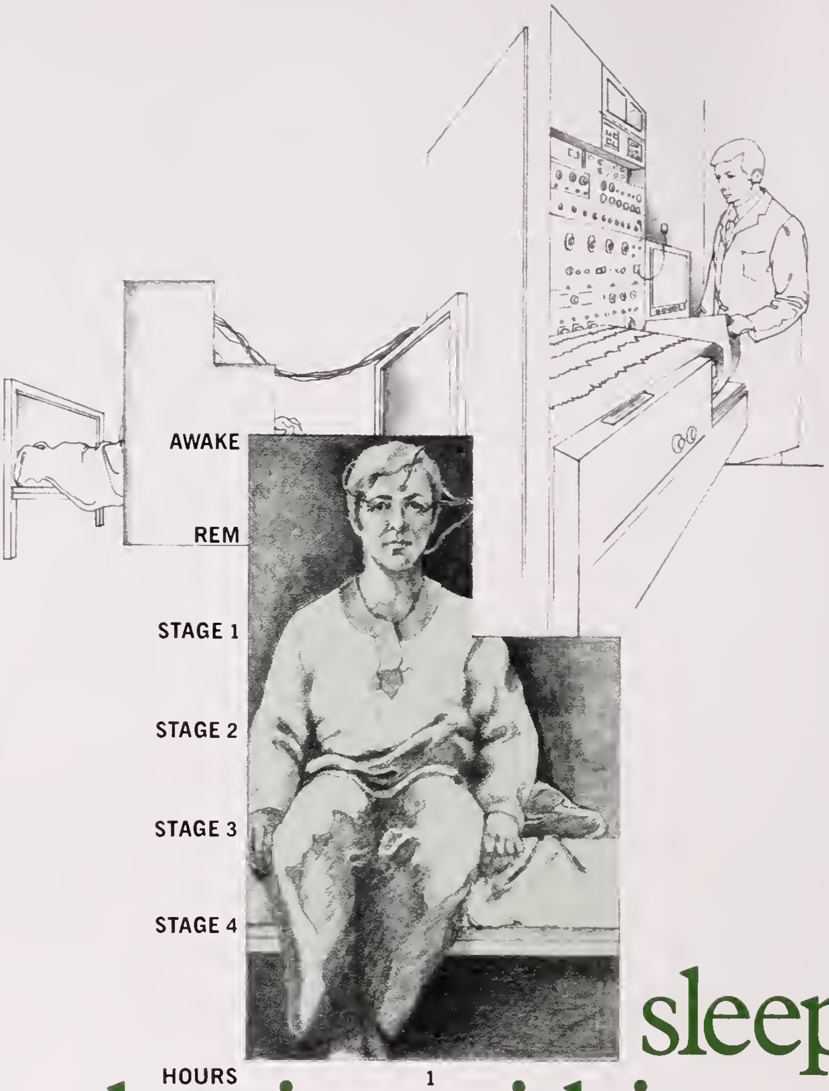

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17 minutes, on average...
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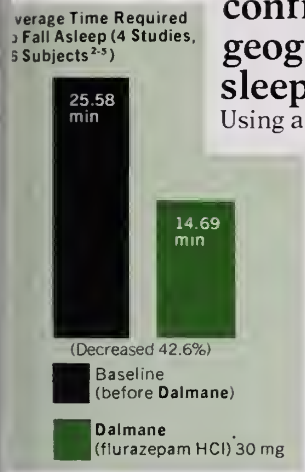

confirmed by clinical studies in four geographically separated sleep research laboratories[2-5]

Using a 14-night protocol involving eight insomniac and eight normal subjects, four studies confirmed the sleep-inducing effectiveness of Dalmane (flurazepam HCl) and the reproducibility of this response. On average, one 30-mg capsule induced sleep within 17 minutes. In all these studies, Dalmane induced sleep rapidly, reduced nighttime awakenings, and provided 7 to 8 hours of sleep without repeating dosage.[2-5]

Dalmane (flurazepam HCl) induces and maintains sleep, with relative safety

almane is generally well tolerated; morning "hang-over" has been relatively frequent. While dizziness, drowsiness, lightheadedness and the like have en noted most often, particularly in the elderly and debilitated, physicians ıould be aware of the possibility of more serious reactions, as noted below.

fore prescribing Dalmane (flurazepam HCl), please consult Complete Product Information, summary of which follows:

dications: Effective in all types of insomnia characterized by difficulty in falling asleep, equent nocturnal awakenings and/or early morning awakening; in patients with recurring somnia or poor sleeping habits; and in acute or chronic medical situations requiring restful eep. Since insomnia is often transient and intermittent, prolonged administration is generally ɔt necessary or recommended.

ɔntraindications: Known hypersensitivity to flurazepam HCl.

arnings: Caution patients about possible combined effects with alcohol and other CNS epressants. Caution against hazardous occupations requiring complete mental alertness .g., operating machinery, driving). Use in women who are or may become pregnant only when ɔtential benefits have been weighed against possible hazards. Not recommended for use in ersons under 15 years of age. Though physical and psychological dependence have not been ported on recommended doses, use caution in administering to ddiction-prone individuals or those who might increase dosage.

recautions: In elderly and debilitated, initial dosage should be mited to 15 mg to preclude oversedation, dizziness and/or ataxia. combined with other drugs having hypnotic or CNS-depressant fects, consider potential additive effects. Employ usual precautions patients who are severely depressed, or with latent depression or ıicidal tendencies. Periodic blood counts and liver and kidney ınction tests are advised during repeated therapy. Observe usual recautions in presence of impaired renal or hepatic function.

dverse Reactions: Dizziness, drowsiness, lightheadedness, aggering, ataxia and falling have occurred, particularly in elderly r debilitated patients. Severe sedation, lethargy, disorientation and ɔma, probably indicative of drug intolerance or overdosage, have een reported. Also reported were headache, heartburn, upset omach, nausea, vomiting, diarrhea, constipation, GI pain, nervousess, talkativeness, apprehension, irritability, weakness, palpitations, hest pains, body and joint pains and GU complaints. There have lso been rare occurrences of sweating, flushes, difficulty in focusing, lurred vision, burning eyes, faintness, hypotension, shortness of reath, pruritus, skin rash, dry mouth, bitter taste, excessive salivaon, anorexia, euphoria, depression, slurred speech, confusion, estlessness, hallucinations, and elevated SGOT, SGPT, total and irect bilirubins and alkaline phosphatase. Paradoxical reactions, g., excitement, stimulation and hyperactivity, have also been eported in rare instances.

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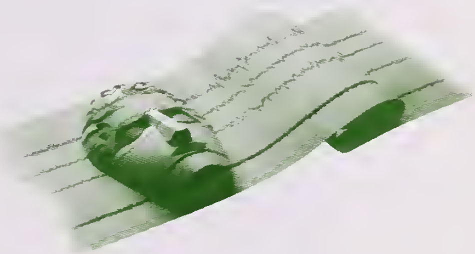

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EFERENCES: 1. Kales A, *et al*: *Arch Gen Psychiatry 23*:226-232, Sep 1970
. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and leep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric ssociation, Washington DC, May 3-7, 1971
. Frost JD Jr: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ
. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ
. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc, Nutley NJ

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OUR COVER

Great veins of gold and silver drew men with high hopes to central Nevada where the Sutro mines were among the greatest in the West. Belmont was then the county seat of Nye County, Nevada, but when the mines flooded in 1892, there was neither fertile soil nor a congenial climate to make the miners linger. Tonopah became the county seat, and Belmont another town that lived the pathetic, recurrent legend of expectations gone awry. Credit: Tony Mendlin.

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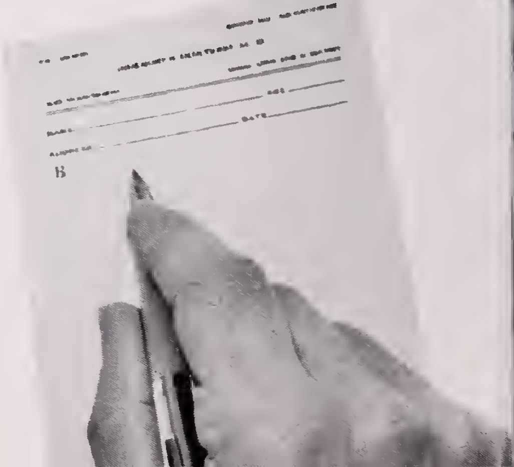
Bioequivalence



he weight of scientific opinion:

If the pharmacist substituted a emically equivalent drug for the e you have specified for your tient—could you be certain of that oduct's safety and effectiveness nply because the chemical content as the same?

Definitely not, unless bio- uivalence tests and other quality surance checks had been conducted. ne pharmaceutical industry and any scientists have maintained this sition for years, but others have estioned it. Now the Office of chnology Assessment of the ongress of the United States has ported on the issue in its Drug oequivalence Study.*

Here are a few definitive state- ents in the O.T.A. report:

"...the problem of bioinequiva- ncy in chemically equivalent prod- ts is a real one. Since the studies in hich lack of bioequivalence was monstrated involved marketed oducts that met current compen- al standards, these documented in- ances constitute unequivocal idence that neither the present andards for testing the finished oduct nor the specifications for aterials, manufacturing process, d controls are adequate to ensure that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.

DRUG
BIOEQUIVALENCE

A REPORT OF THE
OFFICE OF TECHNOLOGY ASSESSMENT
DRUG BIOEQUIVALENCE STUDY PANEL

"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and (b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or (c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...

P·M·A

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

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*Saturated	2 grams
*Cholesterol	0 (0. per 100 grams)
Sodium	120 milligrams (865 mg./100 gm.)

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Percent of calories from fat	over 99%
**Polyunsaturated	3 grams
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**Cholesterol	0 (0. per 100 grams)

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fore prescribing, see complete prescribing ormation in SK&F literature or *PDR*. The lowing is a brief summary.

lications: Edema associated with congestive art failure, cirrhosis of the liver, the nephrotic ndrome; steroid-induced and idiopathic ema; edema resistant to other diuretic ther- y. Also, mild to moderate hypertension.

ntraindications: Pre-existing elevated serum tassium. Hypersensitivity to either com- nent. Continued use in progressive renal or patic dysfunction or developing hyperkalemia.

arnings: Do not use dietary potassium supple- nts or potassium salts unless hypokalemia velops or dietary potassium intake is markedly paired. Enteric-coated potassium salts may use small bowel stenosis with or without eration. Hyperkalemia (>5.4 mEq/L) has en reported in 4% of patients under 60 years, 12% of patients over 60 years, and in less an 8% of patients overall. Rarely, cases have en associated with cardiac irregularities. cordingly, check serum potassium during erapy, particularly in patients with suspected confirmed renal insufficiency (e.g., elderly or abetics). If hyperkalemia develops, substitute hiazide alone. If spironolactone is used con- mitantly with 'Dyazide', check serum potas- ım frequently—both can cause potassium re- ntion and sometimes hyperkalemia. Two aths have been reported in patients on such mbined therapy (in one, recommended dosage as exceeded; in the other, serum electrolytes ere not properly monitored). Observe patients 'Dyazide' regularly for possible blood dys- asias, liver damage or other idiosyncratic actions. Blood dyscrasias have been reported patients receiving Dyrenium (triamterene, K&F). Rarely, leukopenia, thrombocytopenia, ranulocytosis, and aplastic anemia have been ported with the thiazides. Watch for signs of npending coma in acutely ill cirrhotics. Thia- des are reported to cross the placental barrier nd appear in breast milk. This may result in tal or neonatal hyperbilirubinemia, thrombo- ytopenia, altered carbohydrate metabolism nd possibly other adverse reactions that have ccurred in the adult. When used during regnancy or in women who might bear hildren, weigh potential benefits against ossible hazards to fetus.

recautions: Do periodic serum electrolyte and UN determinations. Do periodic hematologic tudies in cirrhotics with splenomegaly. Anti- ypertensive effects may be enhanced in post- ympathectomy patients. The following may ccur: hyperuricemia and gout, reversible itrogen retention, decreasing alkali reserve vith possible metabolic acidosis. hypergly- emia and glycosuria (diabetic insulin require- ents may be altered), digitalis intoxication (in ypokalemia). Use cautiously in surgical pa- ients. Concomitant use with antihypertensive gents may result in an additive hypotensive ffect.

dverse Reactions: Muscle cramps, weakness, lizziness, headache, dry mouth; anaphylaxis; ash, urticaria, photosensitivity, purpura, other lermatological conditions; nausea and vomiting may indicate electrolyte imbalance), diarrhea, onstipation, other gastrointestinal disturbances. Rarely, necrotizing vasculitis, paresthesias. cterus, pancreatitis, and xanthopsia have ccurred with thiazides alone.

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Malpractice Insurance—The Options

William K. Stephan, MD, President of the Nevada State Medical Association, is the author of a recent letter to the membership of that society entitled "Professional Liability Insurance—A Status Report." The paper, dated January 13, 1975, was an indepth analysis of the Nevada problem by an expert. Much of the background information is no longer news, since every physician is now aware of the threat of monstrous increases in malpractice premiums because of the problems of the carriers. Part of the analysis is mainly of interest to Nevada physicians, who have already received the report. Some of Dr. Stephan's report should be informative and perhaps helpful to all physicians.

For several years the NSMA has had sophisticated, organized, active direction of malpractice insurance through an arm of their society, the Professional Liability Management Council. Through this organization the doctors make the specifications and govern the quality control of the protection plan, while the insurance carrier sets the price and provides the bankroll. The group program has been carried by Argonaut Insurance Company, a major carrier who was sensitive to the problems of the physicians and willing to risk the participation in management by a practicing medical insurance committee. To us, the fact that such a well-organized program faces dissolution of the contract with the carrier on May 1, 1975 points up the magnitude of the crisis in liability coverage.

Dr. Stephan's report sets forth the options for the Professional Liability Management Council. (1) Accept the new rates. (2) Deal with a new carrier and risk loss of some of the improvements resulting from physician management by the council. (3) Set up a program of self-insurance, a physician co-op managed by top-rate professional insurance people, a proposition which would require unanimous participation and full acceptance of rules and rates — not hallmarks of the usual medical organization. Finally, (4) there are the legislative options, and we quote:

> As all of you know, there is no staff room without its discoverer of the "no-fault" or the "airline flight insurance" solution to malpractice problems, not to mention the "let's march on Carson City" or "let's strike" promoters. All of us can sympathize with the activist, the person with the timely diagnosis and aggressive therapy. Please believe that I do not deprecate the efforts and motivations of such concern. There *is* a place for legislative and political action.
>
> There is nothing new about "no-fault" or "airline flight" insurance or "workmen's comp" type of malpractice proposals. To be brutally frank, all that these proposals would accomplish would be to make two sources of money available to victims (or claimed victims) of negligence. There is no constitutional way that any of these mechanisms can reward the "victim" that excludes his right to seek further redress for damages that he claims were the result of negligence. Perhaps, psychologically, some injured or otherwise aggrieved persons will be less inclined to seek further recompense if they have already received one award, but there is no reason to be optimistic about this. No-fault automobile insurance has not reduced automobile insurance premiums nor reduced to any noticeable extent the activity of plaintiff attorneys seeking personal injury awards for accident victims.
>
> We *might* in the legislature achieve the introduction of the problem. We *might* get, hand in hand with the Bar Association, legislation to force all proposed malpractice actions to be screened by the medical-legal screening panels

> (which have great success in discouraging non-meritorious cases). We *might* generate enough factual material about what kind of cases get awards when there is only technical (not medical) negligence, that the public conscience is offended. We *might* get publicity enough to convince the public that the cost of liability insurance is a consumer concern. The results of educational programs are notoriously slow.
>
> forward:
>
> The ultimate logic will come not from the control of "greedy lawyers" or "opportunistic insurance carriers" or even marginal doctors, but from juries that find some other way than plundering doctors' insurance carriers to relieve the social tragedies they see in court.
>
> The professional liability part of our lives is terribly irksome, whether we call it a crisis or whatever. It looks as if it will not be less so for years to come. In this hostile socio-legal and financial milieu, there are some solutions, I believe, although none of them is ideal or even pleasant. All over the country, medical societies are attempting to do cram studies of the genesis of their insurance plight, its dimensions and its possible resolution. None of these efforts by medical societies has the advantage we have here in Nevada by being part of the Physicians Liability Management Council that has more know-how and contracts than any group of physicians anywhere working on the problem. I am completely satisfied that if there is a solution, PLMC will find it.

These are the opinions of an expert.

Can We Afford It?

There is nothing that is all bad, and this old adage applies even to a recession. Some good will perhaps result from our present economic setback. The type and scope of activity of a society is determined by the economy. The economics of a democracy are an important influence in keeping it realistic. It seems obvious that the present flurry of debate about our position in Vietnam and Cambodia, a long overdue decision, was precipitated by the state of our economy. Over the past few months, corruption in government, extravagance of congressmen, boondoggling, and political back-rubbing have become increasingly common news. The cost of things in government has now become important.

Before the massive intervention of government into the health field, the economics of medical care was a major determinant of, for whom, and how much. Implementation of Medicare abolished many of the economic limitations. However, many physicians have always known that there is a financial limit to the amount of medical care that the nation can support. Some have even stated as much, but during the prosperous past decade it was impossible for any question of monetary ceiling to get an audience larger than the doctors' cloak room. Hubert Humphrey proclaimed that in this wealthiest nation in the world no price was to high for first class health care for everyone—and nobody wanted to hear any other tune. But now in our sagging economy it becomes possible for doctors, hospital administrators, and health professionals to question how much health care America can afford.

Now we are beginning to hear discussions and to read articles which ask about fiscal limits to health care. Even HEW is worried and concerned, although, of course, the liberals in Congress will be the last to accept the news. It is now possible for the president of the American Hospital Association to ask the question "How Much Care Can We Afford?", the title of an article in *Prism*, October 1974. Of course this paper primarily addresses itself to the problems of hospitals trying to survive and the problems of government trying to handle its promises to Medicare and Medicaid. It doesn't approach the basic issue of whether any nation has the wealth to support Hubert Humphrey's dream or to satisfy Senator Kennedy's political ambitions. But at least the question can now be asked, and the forum for the discussion is the nation. It's a start.

Cranial expansion cyst and headache

Donald R. Olson, MD, Thomas W. Kavanagh, MD, and
Ernest W. Mack, MD, Reno, Nevada

CHRONIC, UNREMITTING, DULL, frontal or posterior headache, as a primary symptom, remains a common patient complaint. In the process of evaluation, the source of pain in the majority of these patients is said to be extra-cranial and, more appropriately, extracerebral. Unquestionably, headache originating from within or around the cervical spine, (muscle spasm, tension, etc.) remains the most frequent type. In the discussion of frequency regarding the symptom complex, it remains all too easy to ignore other extracerebral or intracranial pain sources, in particular, the sella turcica, frontal and sphenoid sinuses. Acute or chronic sinusitis, with fluid levels or opacification noted on x-rays, are seldom a diagnostic problem. The purpose of this paper is to present a series of cases, all presenting in a predictable manner, all manifesting expansile cysts or mucoceles within the sinus or sella, and all with a primary complaint of headache.

CASE REPORTS

Case 1: A 42-year-old, white, airline pilot presented with a 14-year history of frontal headache. Fourteen years ago, the patient was involved in a two car automobile accident where he sustained dashboard trauma without other serious personal injury. Intermittently since, severe headache, noted particularly on descent from altitude, has been present. Sinus x-rays have repeatedly been read as normal, with only questionable thickening of the mucous membrane. Frontal sinus exploration showed a large, right, frontal mucocele (Fig. 1), with definite obliteration of the nasal frontal duct. Six months after frontal sinus surgical obliteration with free fat graft, the patient has returned to flying without pain.

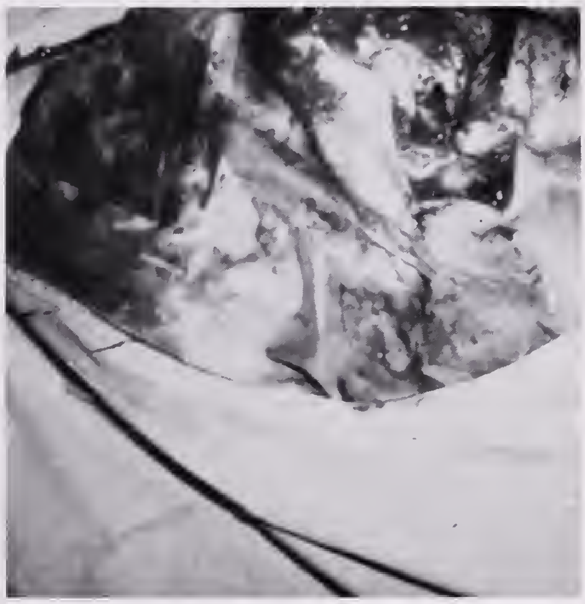

Fig. 1. Frontal sinus mucocele demonstrated at surgery.

Case 2: A 24-year-old female nurse, some six years prior, was involved in a severe automobile accident, sustaining dashboard injury with associated facial lacerations and resultant blindness of the right eye. Intermittent, intense, frontal headache persisted. RISA cisternography (radioactive iodine study) showed active rhinorrhea with intrasinal uptake. Craniotomy obliterated persistent cerebrospinal fluid fistula, but frontal sinus headaches persisted. Frontal sinus exploration showed a non-healed fracture extending through the inner frontal sinus wall with a persistent arachnoidal fistula and cerebrospinal fluid leaking directly into an intrafrontal sinus cyst. Frontal sinus evacuation and obliteration with free fat graft has eliminated the patient's symptoms.

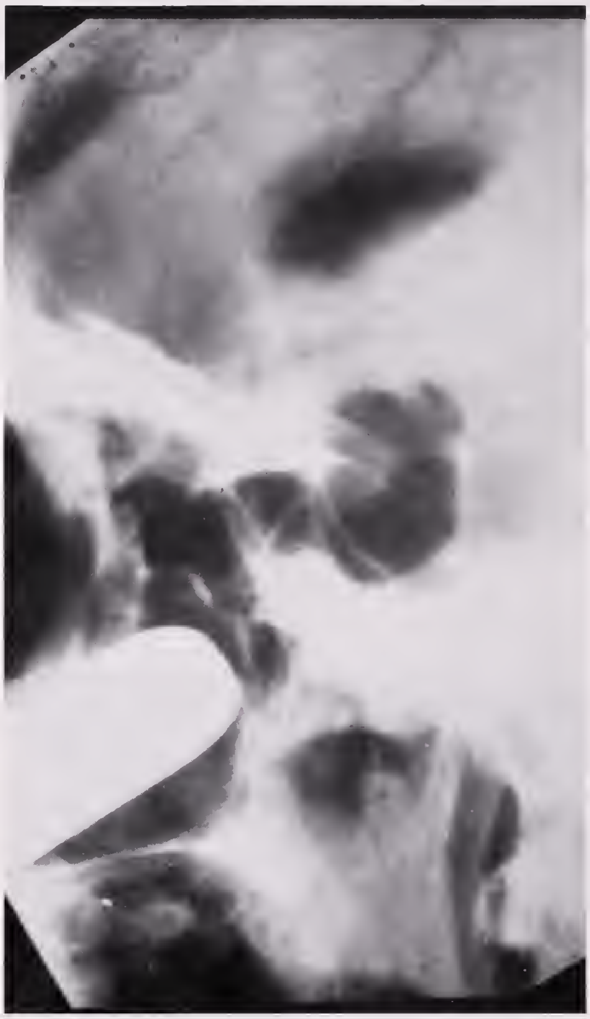

Fig. 2. Intrasellar cyst demonstrated at surgery.

Case 3: A 32-year-old, white, male presented with intense frontal headache with noted sphenoid sinus clouding on tomography. After five days intensive intravenous antibiotic therapy, all head pain had subsided. Additional antibiotic coverage and avoidance of barotrauma over the next ten days completely cleared all symptoms, and the x-ray tomography returned to normal.

Case 4: A 33-year-old, white, male golf professional presented with intense frontal headache which had existed from four to five years, worsening over a two months period. Two years prior, the diagnosis of hyposecretory pituitary tumor had been clinically established and treated with x-ray cobalt therapy. Transsphenoidal surgical exploration showed an intrasellar expansion cyst with an empty sella (Fig. 2). Surgical obliteration of the sella with free fat and bone graft with muscle has eliminated all symptoms. Three years post surgery, the patient has now returned to his full golfing schedule, completely symptom free.

Mucocele

Mucocele, meaning a mucus retaining cyst, is not a completely accurate definition as applied in this connotation. Expansile cysts within the sinus, or within the sella turcica, is more appropriate. Expansion and epicranial

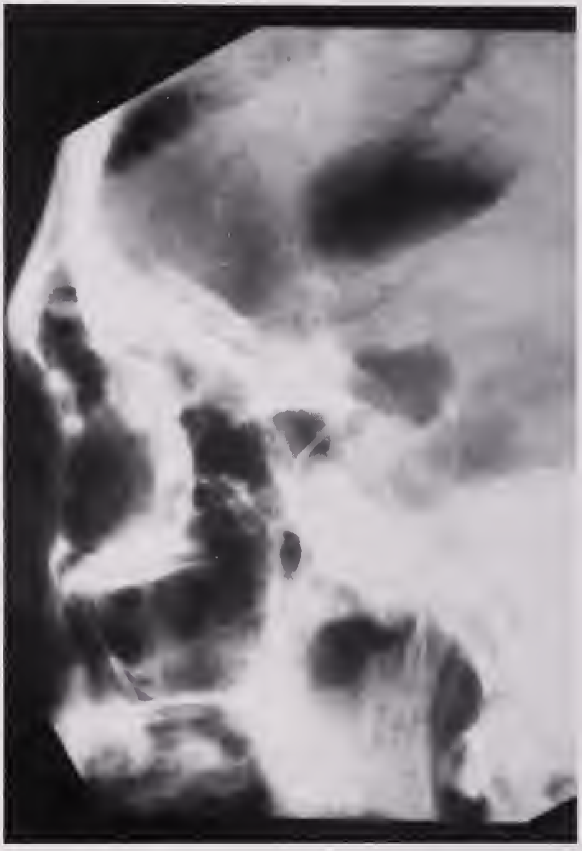

Fig. 3. Post obliteration intrasellar cyst.

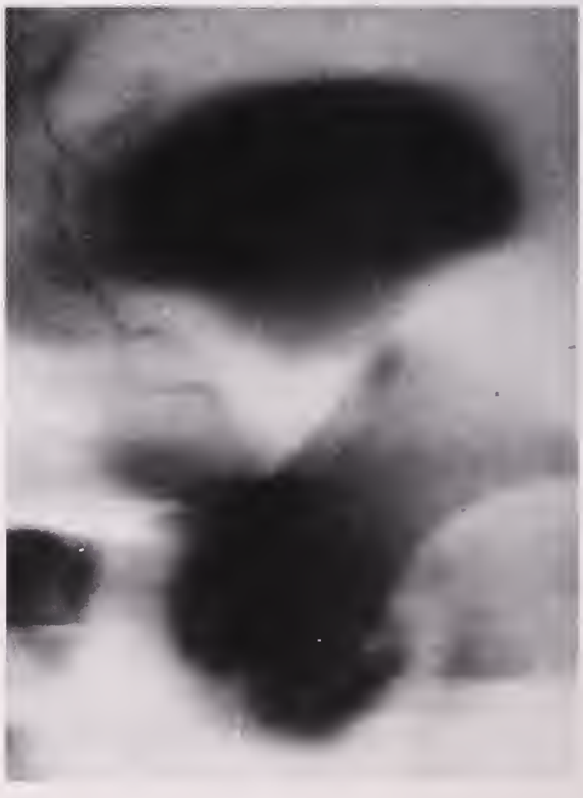

Fig. 4. Post-surgical empty sella.

irritation is a strong source of pain, as is known to anyone who has experienced sharp, frontal pain after holding a cold substance, such as ice cream, against the upper hard palate. Trauma preceding the symptoms remains a frequent cause, though not exclusive. Frontal fractures, with shearing forces causing obstruction directly or inadvertently through slowly evolving fibrosis of the frontal nasal duct, is a common entity with dashboard injuries. Associated, commonly, are fractures through the inner sinus wall with actual cerebrospinal fluid fistulae extending through the fracture line. Allowed to exist for an extensive time, actual intrasinal leptomeningeal cysts are a distinct possibility. Within the sella turcica, prior pituitary tumors, aggressively treated, produce empty sellae (Fig. 4). Expansion, with transmitted pulsations, produces a regular chronic syndrome of headache, described as dull and unremitting, existing back to the center of the head with some transmission to the top of the head. With severity, visual symptoms may be associated. These may exist, either by downward migration of the optic chiasm into an empty sella, or by upward subluxation of a normal pituitary against the optic chiasm, producing visual field defect.

Summary

Demonstrable cases have been presented for the purpose of elucidating seldom considered causes of a common complaint. Specific tests, such as tomography, cisternography, and pneumoencephalography, are helpful, yet, still, the diagnosis often remains elusive. Surgical treatment, with evacuation and obliteration with free fat graft, offers a cure in most cases.

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Cardiac care in a community hospital

Jerry N. Zebrack, MD, and Ann Pennelle, Reno, Nevada.

It is important in all aspects of medicine to periodically review the statistics concerning various medical problems. This paper is a review of the Coronary Care Unit morbidity and mortality at Washoe Medical Center in Reno, Nevada. Records of 100 consecutive patients were reviewed and compared with data reported from other Coronary Care Units throughout the country.

Washoe Medical Center is a community hospital with approximately 430 acute care beds. The hospital is located in the center of Reno, Nevada, with a surrounding population of approximately 100,000. There is a referral population in excess of 300,000, the area encompassing all of Northern Nevada and portions of adjoining California.

The Coronary Care Unit consisted of nine acute monitoring beds in three separate rooms, and eight convalescent, nonmonitored beds. There are over two hundred physicians in Reno, Nevada, all of whom may admit to the Coronary Care Unit. The majority of patients admitted to the Coronary Care Unit are from a group of approximately thirty physicians, who form the nucleus of physicians taking care of patients with acute myocardial infarction.

The Coronary Care Unit is staffed by specially trained registered nurses and their assistants. There are routine orders to give emergency care such as cardiopulmonary resuscitation, electrical cardioversion, and intravenous Lidocaine or Atropine as the situation requires. There is an ongoing medical educational program for the nurses with constant review and educational material being presented. There is also a yearly review course for the nurses presented by the hospital and staff physicians.

There are approximately 16,000 hospital admissions to Washoe Medical Center yearly, with an average of 60 admissions to the Coronary Care Unit per month.

Methods

Beginning in April, 1972, all of the charts of patients admitted to the Coronary Care Unit were reviewed until 100 consecutive patients were obtained who had a definite diagnosis of acute myocardial infarction. These charts were reviewed by at least two of the authors.

The criteria for the diagnosis of acute myocardial infarction included a compatible clinical history, the development of diagnostic Q waves, characteristic evolution of ST segments, and T wave abnormalities on the EKG, and typical serial cardiac enzyme changes of CPK, SGOT, and LDH. Patients who did not meet all of the above criteria were excluded.

To compile the incidents of arrhythmias, all monitor strips and nursing notes were reviewed from the stay in the Coronary Care Unit. If an individual patient had more than one type of arrhythmia, each arrhythmia was categorized separately, thus there were more arrhythmias than there were numbers of patients.

Shock is defined as the presence of a blood pressure less than 90 mm Hg. (systolic), a low or absent urinary output, with peripheral constriction that persisted for 12 hours, or more, following admission.

There were several patients who expired before typical evolutionary changes in the EKG or cardiac enzymes were obtained. If the evidence was compatible with that of acute myocardial infarction, these were included in the group. There were three such patients.

All patients had a detailed admission and physical examination on their charts, and these were reviewed to obtain the past medical history and details concerning their present problem. Because of the retrospective nature of the study, no patients were individually interviewed.

TABLE 1
MORTALITY BY AGE AND SEX

Age Group	Male	Female	Total	Mortality Male	Mortality Female	Total
20-29	1	0	1	0	0	0
30-39	2	0	2	0	0	0
40-49	21	3	24	1	0	1
50-59	26	9	35	2	1	3
60-69	16	9	25	1	1	2
70-79	5	4	9	1	2	3
80-89	2	2	4	1	1	2
Total	73	27	100	6	5	11

The diagnosis of heart failure was based on the physicians' notes and x-ray reports. Diagnostic criteria for heart failure included an S3 gallop, pulmonary rales, peripheral edema, and chest x-ray findings of pulmonary vascular congestion.

Results

Patients were divided into groups on the basis of age and sex, as can be seen in Table 1. The majority of the patients admitted to the Coronary Care Unit were male. The mortality among the male patients was only 8 per cent as compared to 19 per cent for the women. The mortality was 38 per cent for those over the age of 70 as compared to 5 per cent for those under 70 years of age.

The incidents of arrhythmias was related to the site of myocardial infarction, as can be seen in Table 2. There was no predominant arrhythmia for the various localities of the myocardial infarction. The per cent of patients with V.T. or V.F. were similar in the group of patients with an inferior as compared to anterior myocardial infarction. As a group, individuals with anterior septal, anterior, and anterior lateral myocardial infarctions had a mortality of 18.4 per cent as compared to 5.5 per cent for inferior and posterior myocardial infarctions.

The maximum SGOT rise (Table 3) was arbitrarily divided into three groups, plus the group where the patient expired before a maximum SGOT could be obtained at 48 to 72 hours. The greatest number of patients with a myocardial infarction in the study had a maximum SGOT between 100 and 300. Those with an SGOT greater than 300 had a mortality of 25 per cent against the overall mortality of 11 per cent. It is remarkable that patients with SGOT in the lower values of 40 to 100 had a mortality of 9 per cent versus 4 per cent in the middle range group.

Pacemakers were inserted in 16 patients. The group requiring pacemakers had a mortality of approximately 20 per cent. The mortality was not significantly different between patients with inferior and anterior myocardial infarctions requiring pacemakers. Of those with anterior myocardial infarctions there were three patients with arrhythmias requiring pacemakers. The fourth was inserted for a bifascicular bundle branch block without the development of heart block; this was the only patient in the total group who had a bifascicular bundle branch block.

There were a total of 36 patients who had the findings of congestive heart failure. In that group, eight expired with a mortality of 22 per cent. In addition, there were seven patients with a clinical diagnosis of shock for 12 or more hours following admission. Of these, six expired.

Table 4 is a summary of the major complicating diseases in this group of patients. There were 29 patients who had a diagnosis of prior myocardial infarction. Of these, four, or 14 per cent expired, which is not significantly

TABLE 2
SITE OF INFARCTION AND TYPE OF ARRHYTHMIAS

Site of MI	No. of Patients	Total Arrhythmias	V-Tach	V-Fib	Atrial	S-Tach	S-Brady	Heart Block			Deaths
								1°	2°	3°	
Anterior Septal	3	4	0	0	1	0	0	0	0	0	0
Anterior	26	20	3	1	2	6	1	0	1	0	6
Anterior Lateral	9	5	2	0	0	1	0	0	1	0	1
Inferior	44	36	5	3	2	7	8	1	4	3	3
Posterior	10	8	1	0	1	2	2	2	0	0	0
Partial Thickness	4	2	0	0	0	0	1	0	1	0	0
Combined	3	4	0	0	1	1	1	0	1	0	0
Undetermined L.B.B.B.	1	1	0	0	0	0	0	0	0	0	1

TABLE 3

RELATION OF SGOT TO MORTALITY

SGOT	No. of Patients	Mortality	% Mortality
Died before 48 hours	3	3	100%
40-100	33	3	9%
100-300	52	2	4%
Greater than 300	12	3	25%

greater than the overall mortality. The presence of hypertension, diabetes, or lipid abnormalities prior to admission did not appear to increase mortality.

Conclusions

The overall mortality of 11 per cent compares favorably with the best results previously published. Most Coronary Care Units' mortality figures are in the area of 14 to 16 per cent. [1,2]

When considering the patients who expired for possible characteristics which would identify the high risk grade patient and thus possibly alter the clinical course, our findings are not different from those previously published.[3,4,5]

Certainly, the patient who remains in cardiogenic shock 12 hours following admission is at a very high risk, and in these cases, seven out of eight patients expired. This extremely high mortality has been reported previously and ranges from 80 to 100 per cent in all series. Despite the institution of Coronary Care Units with sophisticated monitoring equipment and specially trained nurses, the presence of shock and the resultant high mortality has not changed. In retrospect, no regimen could be considered superior. The most common method of treatment was a combination of digitalis, norepinephrine, diuretics, and oxygen, with or without isuprel. Also those patients with SGOT greater than 300, reflecting a large amount of myocardial damage, remained at high risk, with a mortality of 25 per cent.

TABLE 4

SUMMARY OF MAJOR COMPLICATING DISEASES

Complicating Diseases	No. of Patients	Mortality	Percent Mortality
Hypertension	12	0	0%
Lipid Abnormality	10	1	10%
Diabetes	14	1	7%
Old MI	29	4	14%
Combined (2 or more of above)	2	0	0%

It was surprising that in the group of 29 patients with prior myocardial infarctions, there were only four deaths, with a mortality of 14 per cent. This has usually been thought to denote a much more serious situation. In considering patients with hypertension, lipid abnormalities, or diabetes mellitus, again no higher mortality was noted when compared to the remainder of the patients.

The age range and distribution of patients is similar to those previously published.[5] It was interesting that in our group of patients, a much higher mortality in women than in men was found. An explanation for this could not be derived by the facts available from the medical charts. The higher mortality in women has been reported by some studies[4] but not in others.[6] The increased mortality in patients over the age of 70 has been previously noted and appears to be related simply to inherent problems associated with aging. No distinguishing complications or problems could be separated by age alone.

Patients with an acute myocardial infarction involving a large area with an SGOT over 300, with or without CHF, especially if cardiogenic shock is present, are at a very high risk. At this time there does not appear to be any immediate solution to that problem. Hopefully in the future with newer modalities of treatment such as counterpulsation or immediate coronary artery surgery, this high mortality can be decreased. Studies are presently being performed to evaluate those possible modes of therapy.

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Essential hypertension in children?

Larry G. McLain, MD, Denver

Evidence is accumulating which suggests that many of the factors which relate to essential hypertension in adults have their onset in childhood.

There has been an abundance of material published recently concerning hypertension, including many articles in the lay press. It has been estimated that 23 million adult Americans have elevated arterial blood pressures, and this group is at high risk for stroke, heart disease, and kidney failure. Thus, it is obvious that hypertension and its associated morbid complications constitute one of the major health hazards in this country. There has been an historic reluctance by physicians to treat elevated blood pressures mainly because of the relative lack of evidence that treatment is significant, but recent evidence[1] has pointed to the efficacy of lowering elevated blood pressures in adults, including those levels previously considered to be mild. However, there is little evidence in the literature concerning the long term implications of elevated arterial blood pressures in children. With the recent surge of interest in hypertension in adults, and because there is little known concerning its etiology and genesis, perhaps more time and effort should be spent investigating this condition in children.

It is generally accepted that most hypertensive adults have essential hypertension, and it has long been held that hypertension in children is rare and, of those children who are found to be hypertensive, most of them will have secondary hypertension. However, a recent study[2] casts significant doubt on this contention. Seventy-four hypertensive children, ages 4 to 18, were thoroughly studied, and the overall incidence of essential hypertension was 93 per cent. Although most of the investigative work regarding the epidemiology of essential hypertension has related to adults, evidence continues to mount that essential hypertension may have its onset in early life.[3] Many factors have been implicated as playing a role in the epidemiology of essential hypertension, including genetic and hereditary influences, atherosclerosis, body stature, dietary salt intake, racial predisposition, and environmental and psycho-social factors.

Genetic and Hereditary Factors

The controversy surrounding genetic versus hereditary influences on essential hypertension has raged for years. It has been shown in laboratory animals that hereditary factors play a significant role in hypertension. For many years Platt[4] has proposed that hereditary factors are the primary cause of essential hypertension and that it relates to a single gene. Contrary to that idea, Pickering[5] believes that blood pressure is influenced by a constellation of genetic factors, which are modified by environmental influences. Further investigation needs to be done in an attempt to determine if a child is born with a certain genetic "makeup" relating to essential hypertension. Biron[6] has partially answered that proposition by investigating families with natural and adopted children and showing that the familial aggregation of blood pressure in childhood is hereditary.

Familial Factors

Evidence continues to accumulate showing a strong familial influence on the development of essential hypertension. These studies demonstrate a familial influence on blood pressure in childhood, and suggest that familial tendencies for hypertension are established early in life. Pediatricians and other physicians delivering primary care to children must be reminded to conduct a thorough family history, looking for the presence of hypertension, stroke, or coronary artery disease in younger family members. If any of these factors are present, these children are at greater risk for developing hypertension.

Atherosclerosis

There have been numerous articles recently concerning the complex interwoven mesh between atherosclerosis and hypertension, particularly as it relates to children. Kannel[7] states that atherosclerosis and hypertension have their origins in infancy and childhood. The exact determining factor of blood lipids and their relationship to hypertension and atherosclerosis are uncertain. There is mounting evidence, however, that excessive dietary fat and carbohydrate intake may play a significant role in the development of atherosclerosis and hypertension. The issue of atherosclerosis can be best placed in its proper perspective by stating that it appears to be a pediatric problem, and that greater emphasis needs to be placed on early detection and perhaps treatment of the child who is at risk for atherosclerosis and hypertension.

Obesity

The relationship between obesity and hypertension has long been recognized. In a comprehensive study relating adiposity and blood pressure by Kannel et al,[8] a higher prevalence of hypertension in the obese patient was found, but obesity was not necessarily the chief determinant factor in those patients who were hypertensive. They also showed that while existing hypertension was related to relative weight, obese patients who were normotensive initially subsequently developed hypertensive cardiovascular disease at an increased rate. In Londe's[2] report of hypertension in apparently normal children he found the prevalence of obesity to be significantly higher in the hypertensive children than in a control group. It is apparent that obesity can be one of the multiple factors relating to etiology of essential hypertension.

Salt

Another factor implicated as a causative factor has been dietary salt intake. Dahl and associates[9] have published several studies suggesting that the level of dietary salt intake may play a role in the development of essential hypertension, and they have postulated that excessive salt intake in infants predisposes them to essential hypertension as adults. They have suggested that salt additives to processed baby foods be discontinued, and others have suggested that infant foods be manufactured which are markedly lower in salt content than those currently available. A recent study of two Polynesian populations with different salt intakes supports Dahl's hypothesis that increased salt intake and higher blood pressures are related. However, a majority of people ingest a large amount of salt without developing hypertension and many hypertensive patients remain hypertensive despite severe salt restriction. In a recent article, the Committee on Nutrition, American Academy of Pediatrics,[10] reviewed current thinking about salt intake and blood pressure in children and made the following statements: (1) "The Committee recommends actions that reduce or avoid increasing the present level of salt intake by children in the population at large. (2) Children with a family history of hypertension may benefit from a low salt diet, although the evidence is incomplete. (3) There is a reasonable possibility that a low salt intake begun early in life may protect, to some extent, persons at risk from developing hypertension." Thus, there is suggestive, but not conclusive, evidence that salt intake plays a role in the development of essential hypertension. It is more than likely one of the main contributing factors in those children who may be genetically predisposed to hypertension.

Race

It has been known for several years that the incidence of hypertensive disease is markedly higher in adult blacks than in adult whites, but there is very little information dealing with this possible racial difference of blood pressure levels in children. Fig. 1 graphically demonstrates the death rates for hypertension by race, showing a strikingly higher death rate for non-whites. Rose[11] recorded blood pressures of 277 Negro children in the tenth grade and compared his results with published data on white children. He found that the mean pressures of the black children were low by comparison with those of the white children. In a more comprehensive and meaningful study, Comstock[12] showed little difference in blood pressures between Negroes and whites up to the age of 15 years, but thereafter at all ages, Negroes had higher mean blood pressure than whites. These studies would suggest that black and white children have comparable blood pressures but at sometime in young adulthood the difference becomes

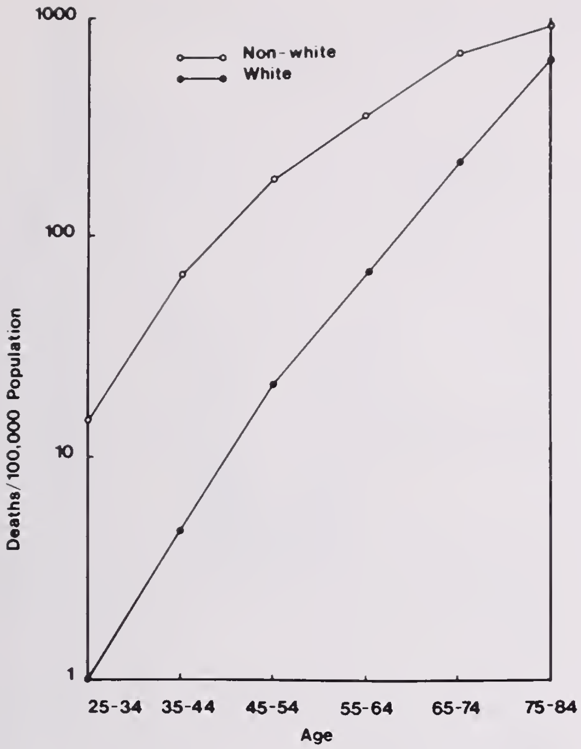

*Fig. 1: Death rates of persons with essential hypertension**

significant. Further investigations need to be done to substantiate this finding. Dube et al[13] measured blood pressures on 1668 black children aged 4 to 17 years. Maximum systolic and diastolic pressures were higher in their group of patients when compared to previously reported results of white children of similar ages. It is apparent there are many unanswered questions relating to racial differences. Longitudinal prospective studies need to be done that answer the following questions: (1) Is there a difference in blood pressures of white and black children when measured under comparable conditions? (2) Is there a form of hypertension to which blacks are particularly predisposed? (3) If blood pressures of black and white children are comparable, what events occur which make adult blacks particularly susceptible to hypertension?

Numerous other factors have been discussed as possibly playing a role in the development of essential hypertension. These include smoking, exercise, environmental surroundings and psycho-social stress.

Summary

It is becoming increasingly apparent that many of the factors which relate to essential hypertension in adults have their onset in childhood. Pediatricians must become more aware of this relationship and must make the recording of a blood pressure an integral part of examination of each child. Those physicians taking care of adults with essential hypertension should spend more time studying and examining the children of these hypertensive parents, because these children may furnish the answer to the enigma of essential hypertension in adults.

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*Chart from "A Study of Blood Pressure Among Negro School Children," Geoffrey Rose, MADM, MRCD, *Journal of Chronic Diseases*, 15,373-380,1962, permission Pergamon Press.

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Urinary prosthetic sphincter

Anthony W. Middleton, Jr, MD, Salt Lake City

An unusual case of urinary incontinence successfully treated by urinary prosthetic sphincter is reported.

SCOTT, BRADLEY, AND TIMM have developed an implantable prosthetic urinary sphincter designed to produce urinary continence in patients previously incontinent.[1-3] Herein reported is a case in which incontinence derived from selective denervation of the urinary sphincter by infection has been controlled by implantation of the prosthetic sphincter.

CASE REPORT

A 13-year-old male was noted to have urinary retention at age seven months of etiology attributed to an "annular constriction of the bladder neck." He underwent a vertical incision in the bladder neck with transverse closure. At age one year an infected mass measuring 3 x 3 cm over the sacrum and felt to be a pilonidal cyst was excised. Two months later he was treated for meningitis, and in the subsequent two months paraplegia gradually developed associated with urinary retention and constipation. At that time a T-10 to L-3 laminectomy was performed with drainage of an intradural abscess. Continued problems over the next six months led to the excision of a lumbosacral extradural inflammatory mass with laminectomy from the sacrum to L-4. Thereafter he remained incontinent of urine and moderately incontinent of stool. In September 1964 another practitioner noted on cystoscopy a "moderately contracted bladder neck" and a valve-like webb extending from the verumontanum to the bladder neck, both of which were resected transurethrally. Thereafter, the patient remained incontinent of urine but bowel control gradually improved to near normal. Continuous catheter drainage was tried beginning in 1970, but was stopped after several months due to continued leakage around the catheter.

In September 1973 cystoscopy showed an essentially normal bladder and urethra, including the external sphincter, except that the sphincter did not wink closed on withdrawing the cystoscope as is usually seen. Neurologic examination showed perineal and perianal anesthesia, depressed cremasteric reflux, diminished sensation in the penis and scrotum, and a somewhat lax anal sphincter. An intravenous pyelogram and voiding cystourethrogram were normal. Cystometrograms performed on three separate days were also normal.

In November 1973 a Kaufman III perineal prosthesis was implanted, with no improvement in continence postoperatively. It was subsequently removed in April of 1974.

On May 2, 1974, a Scott-Bradley-Timm prosthetic sphincter was implanted around the bladder neck anterior to the ampulla of the vas and the seminal vesicles. On the 10th postoperative day the catheter was removed from the bladder and the device was activated. The patient immediately was totally continent with the cuff inflated, and voided with a good stream upon deflating the cuff. A five month followup shows that he remains continent of urine with the exception of occasional nocturnal enuresis, which he attributes to failure on his part to completely inflate the cuff on retiring to bed. He has a normal urinalysis.

Discussion

The Scott-Bradley-Timm prosthetic sphincter has been used in treating urinary incontinence resulting from several etiologies.[1] The types of incontinence successfully treated by the prosthesis include stress, post-prostatectomy, epispadias, urethral trauma and neurologic. The latter includes cases with myelomeningocele, spinal cord injury, multiple sclerosis, atonic bladder of unknown etiology, surgical denervation of the bladder and sacral agenesis, all of which were associated with abnormal bladder function. To our knowledge this is the first case of an incontinent patient with selective neurologic damage to the urinary sphincter but sparing of the bladder innervation successfully made continent by the Scott-Bradley-Timm sphincter. Totally incontinent through all of his life, the patient now has complete control following the implantation.

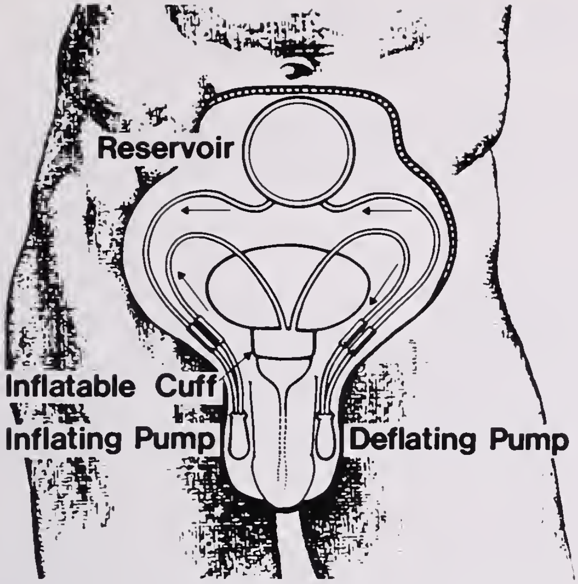

Fig. 1. The Scott-Bradley-Timm prosthetic sphincter. See text for further description.

Fig. 1 outlines the major components of the sphincter. The reservoir is implanted beneath the rectus muscle and is connected by tubing to two pumping bulbs placed subcutaneously in the scrotum (or labia in females). The bulbs in turn are connected by tubing to an inflatable cuff implanted around the bladder neck or urethra. Fluid in the reservoir is pumped by one bulb into the cuff, which then totally occludes the urethral lumen, thereby imparting continence. When micturition is desired the other bulb is pumped to send fluid back into the reservoir from the cuff. The direction of fluid flow is indicated in the diagram by arrows. The valves are designed to maintain a constant, predetermined pressure in the inflated cuff so that continence is maintained but excessive pressure which might produce urethral necrosis is avoided.[3] A whole new technology is evolving concerned with proper patient selection, pre and postoperative management, surgical technics of implantation and subsequent repair of faulty device components.

In this patient we implanted the sphincter at the bladder neck with the cuff in a position that would not occlude the seminal vesicles and ampulla of the vas when the cuff is inflated. This should assure antegrade ejaculation in a normal fashion if the ejaculatory mechanism proves to be intact when this patient passes through puberty, whereas he surely would have had partial or complete retrograde ejaculation into the bladder with no sphincteric function present.

Summary

We have reported a case of urinary incontinence secondary to selective neurologic damage of the urinary sphincter but with normal bladder function. The patient is the first case of its type successfully made continent by the Scott-Bradley-Timm prosthetic urinary sphincter.

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Postoperative hypoxemia at altitude*

Stuart L. Smith, MD, John R. Goodman, BS, ARIT,
Lawrence H. Repsher, MD, Wheat Ridge, Colorado

SIGNIFICANT ARTERIAL HYPOXEMIA following upper abdominal surgical procedures has been well documented at sea level where the normal preoperative pO_2 averages approximately 90 Torr. The present study documents the extent of the decrease in arterial pO_2 in normal patients undergoing gastroduodenal or biliary operations at an altitude of 5,440 feet (1,648 meters), where the normal arterial pO_2 ranges between 65 and 75 Torr. It is not uncommon for the arterial pO_2 to drop to 65 Torr at sea level on the first postoperative day. Although this represents significant relative hypoxemia, this level is only at the lower limit of normal for individuals residing in Denver and is not in the clinically potentially dangerous range. It is of practical interest to know how severe a drop in arterial oxygen tension can be expected at an altitude where the pre-op arterial pO_2 averages only 70 Torr.

Methods

Thirty-four patients admitted consecutively for elective upper abdominal operations at Lutheran Hospital and Medical Center in Wheat Ridge, Colorado were selected by simple questionnaire for symptoms of pulmonary disease. These patients were then screened using a Monaghan 403 Pulmonary Function Analyzer. Despite denying symptoms of pulmonary disease, nine of these patients had pulmonary function test values which were 2 standard deviations or more below predicted normal values and were, therefore, excluded from the study. In the remaining 25 patients arterial blood gases were drawn anaerobically from the radial artery and analyzed by the central laboratory using an IL-313 Blood Gas Analyzer on the day prior to surgery and on the morning of the day following surgery. All patients were breathing room air at the time of the radial artery puncture.

Results

The average preoperative pO_2 of the 25 patients included in the study was 69 Torr. Fourteen of the 25 patients smoked 10 or more cigarettes per day. As a group, the smokers' average preoperative arterial pO_2 was only 65 Torr. The average postoperative arterial pO_2 of all 25 patients was 55 Torr, indicating an average decrease in arterial pO_2 of 14 Torr. The smallest decrement was 1 Torr (68 Torr to 67 Torr). The largest decrement was 28 Torr (70 Torr to 42 Torr). The average postoperative pO_2 for the smokers as a group was 50 Torr, indicating a decrease in pO_2 of 15 Torr. The raw data have been plotted on a scattergraph as shown (Fig. 1).

Discussion

Our data agree with previous published reports of studies done at sea level which have demonstrated average postoperative decreases in arterial pO_2 ranging from 10 to 23 Torr[1-4] (Fig. 2). Our results are significant in three respects. First, patients who deny symptoms of pulmonary disease may well have significant underlying obstructive pulmonary disease. Second, a very low arterial pO_2 that is noted the first two or three days following upper abdominal surgery should be anticipated in all high altitude surgical patients because of the altitude decrement, and does not necessarily indicate that the patient has underlying heart or lung disease. Third, apparently normal patients who have even mild arterial hypoxemia from either heart or lung disease should be anticipated to frequently reach postoperative pO_2 values in the dangerous range after upper abdominal operations at this altitude.

---

* From the Departments of Surgery and Medicine, Lutheran Hospital and Medical Center, Wheat Ridge, Colorado. Dr. Smith is Clinical Instructor in Surgery, University of Colorado School of Medicine, Denver. Mr. Goodman is Clinical Coordinator, Inhalation Therapy School, Community College, Denver. Dr. Repsher is Assistant Clinical Professor of Medicine, University of Colorado School of Medicine, Denver. This study was supported in part by a grant from the Colorado Chapter of the American Cancer Society. Address requests for reprints to: Lawrence H. Repsher, MD, Lutheran Hospital and Medical Center, 8300 West 38th Avenue, Wheat Ridge, Colorado 80033.

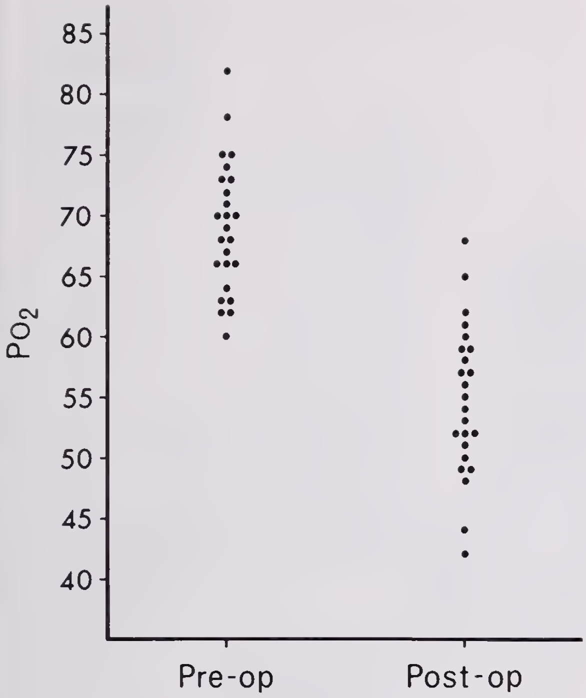
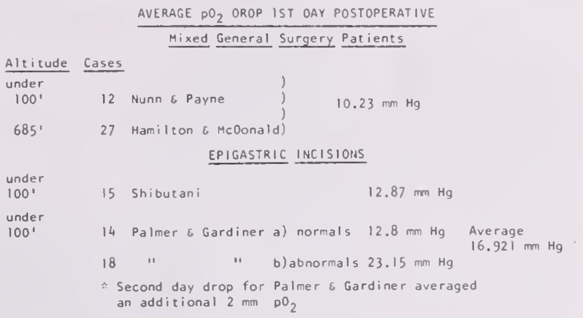


Fig. 1. Preoperative and postoperative pO_2 values of 25 patients who had upper abdominal operations.

At sea level, in patients starting out with a preoperative pO_2 of 90 Torr, there is a built-in reserve which protects these patients who have even large drops in arterial pO_2 postoperatively. The major effect of altitude would appear to be the loss of this reserve. Of significant concern is that 26 per cent of the original 34 patients denied a history of or symptoms of pulmonary disease and yet had significant impairment of pulmonary function as measured by simple spirometry. We have demonstrated that severe hypoxemia can occur even in those patients whose preoperative pulmonary function tests are within normal limits. One would anticipate that a substantial portion of patients whose preoperative pulmonary function testing is abnormal could reach very dangerous levels that might easily go unrecognized, and therefore untreated. We believe our data support the contention that routine preoperative spirometry is indicated prior to major upper abdominal surgery, and that respiratory care is indicated postoperative in those whose preoperative pulmonary function testing is abnormal. Finally, one should be aware that some patients whose preoperative pulmonary function testing is normal may also develop significant arterial hypoxemia. Therefore, any patient who has recently undergone upper abdominal surgery should be observed closely for the often subtle symptoms and signs of hypoxemia, such as mental confusion, agitation, anxiety, and delirium, since obvious cyanosis may not be evident.



AVERAGE pO_2 DROP 1ST DAY POSTOPERATIVE

Mixed General Surgery Patients

Altitude	Cases			
under 100'	12	Nunn & Payne	10.23 mm Hg	
685'	27	Hamilton & McDonald		
		EPIGASTRIC INCISIONS		
under 100'	15	Shibutani	12.87 mm Hg	
under 100'	14	Palmer & Gardiner a) normals	12.8 mm Hg	Average 16.921 mm Hg
	18	" " b) abnormals	23.15 mm Hg	

☆ Second day drop for Palmer & Gardiner averaged an additional 2 mm pO_2

Fig. 2

Summary

Thirty-four consecutive patients admitted for elective upper abdominal surgery at an altitude of 5,440 feet (1,648 meters) were screened preoperatively with a simple questionnaire and routine spirometry. Nine of these patients, or 26 per cent, were found to have spirometric values more than 2 standard deviations below the predicted values for height, age, and sex. The remaining 25 patients with normal pulmonary function were investigated with preoperative and postoperative arterial blood gases. There was an average drop in arterial oxygen tension of 14 Torr with a maximum drop of 28 Torr. The data indicate that at this altitude a significant number of individuals with no history or signs of lung disease may have significantly impaired function after epigastric incisions, and that dangerously low arterial pO_2 levels may be reached postoperatively even in patients with preoperative normal pulmonary function.

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WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

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COLORADO

Epidemiologist Named

Thomas M. Vernon, Jr., MD, chief of epidemiology for the Colorado Department of Health since 1972, has been named head of preventive medical services at the Department, succeeding the late Valentin E. Wohlauer, MD.

Doctor Vernon was graduated from Duke University in North Carolina, and obtained his medical degree from Harvard University. He spent three years with the Center for Disease Control in Atlanta, carried out cholera research in East Pakistan, and advised the Nepal Malaria Eradication Organization. He is a member of the Colorado and Denver Medical Societies and the American Public Health Association.

Chisholm Heads ABFP

Neil Chisholm, MD, Denver, Colorado has been elected vice president of the American Board of Family Practice. He will serve with President George Burket, Jr., MD, Kansas City, Kansas, and newly elected Director James G. Price, MD, of Brush, Colorado, representing the American Academy of Family Physicians.

MEDICAL SCHOOL NOTES

University of Colorado Medical Center

New CU Nursing School Dean

Barbara Redman, MD, associate dean and director of curriculum and instruction, University of Minnesota School of Nursing, Minneapolis, has been selected as the new dean of the University of Colorado School of Nursing; the 38-year-old Dr. Redman will assume her new position Aug. 1, 1975.

Born in Mitchell, S.D., Dr. Redman received her bachelor's degree from South Dakota State University, Brookings, and her master's and doctor of philosophy degrees from the University of Minnesota. She wrote the widely-used textbook, *The Process of Patient Teaching in Nursing*, which has been translated into Japanese and Finnish. She is the author or co-author of more than a dozen other publications.

A 1961-63 recipient of a National League for Nursing fellowship, Dr. Redman is a member of the American Nurses Association and Council of Nurse Researchers and the American Educational Research Association. She also belongs to Sigma Theta Tau, Pi Lambda Theta and Phi Kappa Phi.

Cattle Industry Losses

Brisket disease, a prominent swelling about the breast bone of cattle caused by constriction of the lung, is the subject of experiments with two herds of Hereford cattle being carried out jointly by the University of Colorado School of Medicine and the Colorado State University School of Veterinary Medicine at Fort Collins.

Robert Grover, MD, associate professor of medicine and director of cardiovascular pulmonary research at CU, with John Reeves, MD, CU professor of Medicine, and Donald Will and Archibald Alexander, CSU veterinarians, are collaborating on the study of the non-infectious but sometimes fatal and perplexing ailment, caused by low oxygen pressure.

The disease develops at high altitudes, and is cured at low levels. The three goals of the study are to establish breeding stock adaptable to high altitudes, to set up a treatment program for afflicted cattle, and to educate cattlemen.

* * *

Magnetic Field Probes

The weak magnetic field which each individual generates is being pursued by Martin Reite, MD, associate professor of psychiatry at the University of Colorado School of Medicine. Intensive studies of these currents were initiated by Dr. Reite, along with James Zimmerman of the U.S. Bureau of Standards, Professor Jochen Edrich, electrical engineer at the University of Denver, and John Zimmerman, CU graduate student, late last fall.

Studies are being carried out at the Bureau of Standards in Boulder, in rooms heavily shielded to cut down outside interference capable of altering the MEG or magnetoencephalogram. MEGs and EEGs are collected simultaneously. EEGs measure different voltages within the brain. An MEG measures currents. The comparison suggested by Dr. Reite is that of EEG taking the measure of the different elevations (volts) of a river, versus the size (current) of the MEG.

Dr. Reite believes the MEG "might eventually allow us to look at disturbances in brain function which originate deep within the brain," such as minimal brain dysfunction, as well as alertness of those working in areas of high electrical or magnetic activity.

* * *

Honors to Starzl

Thomas E. Starzl, MD, chairman of the Department of Surgery at the University of Colorado School of Medicine, has been named as one of 30 recipients of 1975-76 faculty scholar awards from the Josiah Macy, Jr. Foundation.

Doctor Starzl's award was the only surgical grant, and he will leave on June 1, 1975 for St. Mary's Hospital Medical School, London, where he will do research in organ transplantation and hepatic physiology. Testing of antigen adjuvants to imnosuppression and further characterization or portal blood hepatrophic factors will also be covered in his studies.

OBITUARIES

Colorado

Ligon Price, MD, died Saturday, December 14, 1974 in the Aspen Valley Hospital at the age of 80 years. Born July 25, 1894 in Pocohontas County, West Virginia, he attended the Green Briar Military Academy in that state, then later the St. Louis College of Physicians and Surgeons in Missouri. He served an internship and residency in surgery at the Denver Presbyterian Hospital and was for five years resident surgeon at Fairmont Hospital, Fairmont, West Virginia.

He opened an office in Hayden, Colorado for the practice of general medicine and surgery in 1937. He served the communities of both Hayden and Mount Harris until he retired to Aspen in 1955.

He was a member of the Mt. Sopris and Colorado Medical Societies, and of the American Medical Association. He was a recipient of the CMS 50-year award. He was very active in the Masonic Lodge and was a member of the Commandery Council of Royal Select Masters. He was a member of the Elks Lodge in Aspen, and of the society of Sons of the Revolutionary War in West Virginia.

He was married to Lucille Jenkinson of Denver in 1938. Mrs. Price survives as do a sister, Mrs. Mary Barlow of Marlinton, West Virginia, and several nephews and nieces.

Richard A. Halverson, MD, of Boulder, Colorado, was killed in a private plane crash near Akron, Colorado on Monday, February 3, 1975. He was the director of the Boulder Community Hospital Emergency Service, a position he held since 1971. Prior to that he resided in Littleton, Colorado. He was president of the Bonded Security Service, Inc. and the Aardvark Aero Associates.

He was a member of the Denver and Colorado Medical Societies and of the American Medical Association, and was a lieutenant commander in the United States Navy Reserves.

He is survived by his parents, Mr. and Mrs. Anton Halverson of Temple, Texas, and a sister, Mrs. J. D. Curran of Cornwall-on-the-Hudson, New York.

Elliott S. Stong, MD, who practiced medicine and surgery in Alamosa, Colorado for over 25 years, died in Medford, Oregon, December 23, 1974 at the age of 82 years. Born in Humboldt, Iowa, October 10, 1892, and educated in the public schools of that city, he attended the University of Iowa where he was awarded both a Bachelor of Science and an MD in 1916. After an internship at the University of Iowa Hospital in Iowa City, he served in the United States Army in World War I.

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Following the war he opened an office in Elkader, Iowa, where he practiced from 1920 until 1924 when he moved to Grand Junction, Colorado. He practiced general medicine and surgery in that city until 1933 when he moved to Alamosa.

He was a member of the San Luis Valley Medical Society, serving one year as its president. He belonged to the Colorado Medical Society and to the American Medical Association. He was on the active staff of the Community Hospital in Alamosa, and was staff president in 1938. Doctor Stong retired from active practice in 1962 and moved to Medford, Oregon.

He was married to Nora E. Daily in Rochester, Minnesota, November 19, 1919. They had three sons, John E., Paul A., and David D. Nora Stong died in 1959. Later he was married to Edith Miller who survives the doctor. David D. Stong, MD, who practiced medicine in Alamosa for ten years, died in 1960. There are nineteen surviving grandchildren.

Montana

Louis Clayton Allard, MD of Billings, Montana died January 8, 1975. Doctor Allard, an orthopaedic surgeon, began his practice in Billings in 1946 with his father Louis, a pioneer orthopaedic surgeon. He had been a member of the Montana Medical Association and the Yellowstone Valley Medical Society since 1947. He was also a member of the American Medical Association and the International College of Surgeons.

He is survived by his wife, Sally, a son, four daughters, a sister and two brothers.

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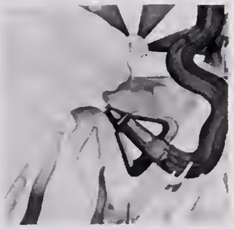

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THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Abdominal Operations: Rodney Maingot. 6th ed. Appleton-Century-Crofts, 1974. 2 vol. $85.00. Gift of Colorado Permanente Group.

Aging and Mental Health; Positive Psychosocial Approaches: Robert N. Butler and Myrna I. Lewis. Mosby, 1973. 306 p. $5.95.

Biofeedback: Behavioral Medicine: Lee Birk, ed. Grune and Stratton, 1974. 209 p. $9.75.

Bronchial Carcinoma: Thomas W. Shields. Thomas, 1974. 181 p. Gift of the American Cancer Society.

The Cervical Spine: Robert W. Bailey. Lea and Febiger, 1974. 263 p. $20.00.

Childbirth Without Fear; The Original Approach to Natural Childbirth. Grantly Dick-Read. Harper and Row, 1972. 420 p.

Current Medical Diagnosis and Treatment: Marcus A. Krupp and Milton J. Chatton. Lange, 1975. $13.50. Review copy.

Diagnostic Ultrasound: Donald L. King, ed. Mosby, 1974. 311 p. $39.50.

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eferences: 1. Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of herapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: lew Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboraories, Inc.

†U.S. Patent No. 2,895,877

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MEETINGS

American Academy of Pediatrics

ANNUAL SPRING SESSION

Denver Hilton, Denver, Colorado

April 14-16, 1975

Contact: Ed Kittreel, Jr., 1801 Hinman Avenue, Evanston, Illinois 60204.

**American College of Surgeons-
American Cancer Society, Colorado Division**

ANNUAL MEETING, AMERICAN COLLEGE OF SURGEONS

The Broadmoor, Colorado Springs, Colorado

April 18-19, 1975

Contact: Mrs. Shirlee Myers, 1601 East 19th Avenue, Denver, Colorado 80218, or call (303) 534-8580.

**Lovelace—Bataan Medical Center—
New Mexico Lung Association**

THE OUTPATIENT DIAGNOSIS AND MANAGEMENT OF COMMON LUNG PROBLEMS

Lovelace—Bataan Medical Center, 5200-5400 Gibson Blvd., Albuquerque, New Mexico

April 18-19, 1975

Contact: Martin J. Conway, MD, Lovelace-Bataan Medical Center, 5200-5400 Gibson Blvd., Albuquerque, New Mexico 87108.

Instrument Society of America

1975 SPRING JOINT CONFERENCE

Queen Elizabeth Hotel, Montreal, Canada

April 24-27, 1975

Contact: Robert Hand, Instrument Society of America, 400 Stanwix St., Pittsburgh, Pennsylvania 15222.

Montana Lung Association

ANNUAL MEETING

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East of Opportunity, Montana**

April 25-26, 1975

Stanford University School of Medicine

MANAGEMENT OF THE SURGICAL PATIENT

Mauna Kea Beach Hotel, Kamuela, Hawaii

April 26-May 3, 1975

Contact: Office of Postgraduate Medical Education, Stanford University, School of Medicine, Stanford, California 94305.

Colorado Academy of Family Practice

13TH ANNUAL SYMPOSIUM—ALLERGIES

Minnequa University Club, Pueblo, Colorado

April 27, 1975

Contact: Samuel Nelson, MD, 129 Colorado Avenue, Pueblo, Colorado 81005.

American Cancer Society-
National Cancer Institute

NATIONAL CONFERENCE ON ADVANCES IN CANCER MANAGEMENT
PART II: DETECTION AND DIAGNOSIS

The Denver Hilton, Denver, Colorado

May 1-3, 1975

Contact: American Cancer Society, 219 E. 42nd St., New York City, NY 10017.

Biennial Western Conference on Anesthesiology

14TH BIENNIAL WESTERN CONFERENCE ON ANESTHESIOLOGY

Princess Kaiulani Hotel, Honolulu, Hawaii

May 4-8, 1975

* * * * *

WORKSHOP

Sheraton Maui Hotel, Island of Maui, Hawaii

May 9-11, 1975

Contact: Murray G. Atnikov, MD, Biennial Western Conference on Anesthesiology, 2574 W. 33rd Ave., Vancouver 13, British Columbia, Canada.

Cardiovascular Department Sunrise Hospital

CURRENT CONCEPTS IN CARDIOLOGY

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May 5-8, 1975

Contact: American Heart Association, 44 East 23rd St., New York City, New York 10010.

New Mexico Medical Society

ANNUAL MEETING

Hilton Inn, Albuquerque, New Mexico

May 14-16, 1975

American College of Surgeons

ANNUAL MEETING, NEW MEXICO-EL PASO CHAPTER

Hilton Inn, Albuquerque, New Mexico

May 17-18, 1975

Contact: William J. Langlois, MD, 717 Encino Place, NE, No. 5, Albuquerque, New Mexico 87102.

American College of Cardiology

ISCHEMIC HEART DISEASE: A CRITICAL OVERVIEW

Golden Gateway Holiday Inn,
San Francisco, California

May 29-31, 1975

Contact: American College of Cardiology, c/o Mary Anne McInerny, 9650 Rockville Pike, Bethesda, Maryland 20014

Rocky Mountain Neurosurgical Society

TENTH ANNUAL MEETING

Hotel Cozumel Cariebe, Cozumel Island, Yucutan Peninsula, Mexico

June 8-11, 1975

Contact: Richard H. Moiel, MD, 601 Medical Towers, 1709 Dryden St., Houston, Texas 77025.

University of Colorado Medical Center

PATHOLOGY IN GYNECOLOGY AND OBSTETRICS

Given Institute of Pathobiology
Aspen, Colorado

June 30 - July 4, 1975

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CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.

WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported. **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**

Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy

Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued.

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Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.

PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin

ADVERSE REACTIONS: Gastrointestinal (oral and parenteral forms): anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.

Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**).

Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**).

Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

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Rocky Mountain Medical Journal

May 1975

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M U S

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The Roundup

The rugged lives of the cowboys culminated annually in the peaking tumult of the roundup.

Rounding up the cattle, cutting out the calves, counting and roping them, pressing them against the ground for branding, and salving the burn—this activity was what the cowboy had trained himself for from his first fledgling experience. The trampled sage mixed with the dust to send up choking clouds through which the cowboys could hardly see what they were doing, but their trained instincts were sharp, and thousands of cattle were branded this way.

To 16-year-old "Kid" Russell, a boy whose wanderlust his family hoped to cure in rugged frontier experience, the roundup was certainly the exciting time depicted on our cover. Russell had gone first with an outfit near Billings as night wrangler. His first cattle drive was into the Judith Basin with over 1,000 cattle.

Russell looked at the cowboys in their wandering frontier life, following the trail, learning the important instincts of self-preservation so that the cattle could he guarded. The Indian was never far away. Wolves and coyotes and eagles threatened the cattle as did blinding blizzards that froze. From this experience Russell acquired the feeling for what he had lived with that made him wish to project a direct image. "The Roundup" like the best of Russell gives us a total experience, enlarged by the artist's close feeling for the West in all its color and drama.

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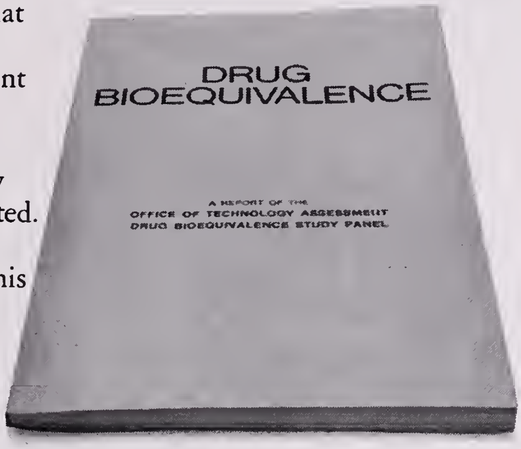

DRUG
BIOEQUIVALENCE

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OFFICE OF TECHNOLOGY ASSESSMENT
DRUG BIOEQUIVALENCE STUDY PANEL

"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and
(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or
(c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription…

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
Washington, D.C. 20005

*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

protecting the ntegrity of your prescription

ROCKY MOUNTAIN MEDICAL JOURNAL

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Letters TO THE EDITOR

To the Editor:

Again, this year I am compiling a Biting Insect Summary and would appreciate any case reports of unusual allergic reactions to biting insects, i.e., mosquitoes, fleas, gnats, kissing bugs, bedbugs, chiggers, black flies, horseflies, sandflies, deerflies, etc.

I would like physicians to supply me with case reports of those patients who have had unusual reactions to such insects. Include in your reports, the type of reactions and complications, if any, the age, sex, and race of the patient, the site of the bite(s), the season of the year, the immediate symptoms, the skin test results, desensitization results, if any, and any associated other allergies. Send this information to the following address — Claude A. Frazier, MD, 4-C Doctors Park, Asheville, N.C. 28801.

Thank you for your assistance.

Sincerely,
Claude A. Frazier, MD

Notice has gone out from the American Board of Family Practice, to diplomates certified in 1970, of procedures and requirements of the 1976 recertification examination, first such mandatory recertification undergone by a group from the ABFP.

The class of some 1,700 diplomates must:

- Take a half-day written examination, October 29, 1976;
- Review 20 patient charts, and submit answers to a set of questions about each prior to the exam.

The charge for the process will be $150, as opposed to the $300 for regular certification.

Two eligibility requirements apply to all diplomates seeking recertification:

- A written statement, which will be corroborated, that the candidate holds unrestricted licensure(s).
- Proof that the candidate has completed 300 hours of acceptable continuing education in the last six years.

Applicants will be notified of their eligibility to sit for the cognitive exam well in advance of the October 29, 1976 examination date. The exam will be offered at five test sites.

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Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis. Known sensitivity. Not recommended in pheochromocytoma. Unsuitable in mild or labile hypertension responsive to mild sedation or thiazide therapy. Use cautiously in patients with history of previous liver disease or dysfunction.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between six and twelve months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at six and twelve months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first three weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first two to three months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first six to twelve weeks of therapy or whenever an unexplained fever occurs. If fever, abnormalities in liver function tests, or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, reversible reduction in leukocyte count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur.

Use in Pregnancy and Childbearing Age—Not recommended in pregnancy. In women of childbearing age, weigh potential benefits against possible fetal hazards.

Precautions: Methyldopa may interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, spuriously high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has occurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: Sedation, usually transient, may be seen during initial therapy or when dosage is increased. Headache, asthenia, or weakness may be noted as early, transient symptoms. Symptoms associated with effective lowering of blood pressure are occasionally seen and include dizziness, lightheadedness, and symptoms of cerebrovascular insufficiency. Angina pectoris may be aggravated. Symptoms of orthostatic hypotension may occur; if symptoms occur, reduction of dosage is suggested. Bradycardia, nasal stuffiness, mild dryness of mouth, and gastrointestinal symptoms including distention, constipation, flatus, and diarrhea occur occasionally; these generally can be relieved by reducing dosage. Nausea and vomiting have been reported in only a few patients. Sore tongue or "black tongue," pancreatitis, and inflammation of salivary glands may occur.

Weight gain and edema occur infrequently and are relieved by administering a thiazide diuretic; if edema progresses or signs of pulmonary congestion appear, discontinue drug. A rise in BUN has been observed. Other rare reactions include breast enlargement, lactation, impotence, decreased libido, skin rash, mild arthralgia, myalgia, paresthesias, Bell's palsy, parkinsonism, psychic disturbances including nightmares, reversible mild psychoses or depression. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Note: Dosage should be limited initially to 500 mg daily when following previous antihypertensive agents other than thiazides. Maximal recommended daily dose is 3.0 g. Patients with impaired renal function may respond to smaller doses than patients with normal kidney function. Syncope in older patients has been related to increased sensitivity in those with advanced arteriosclerotic vascular disease; this may be avoided by lower doses. Tolerance occasionally seen either early or late, but more likely between second and third month after initiation of therapy; increased dosage or combined therapy with a thiazide frequently restores effective control.

How Supplied: Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., INC., West Point, Pa. 19486

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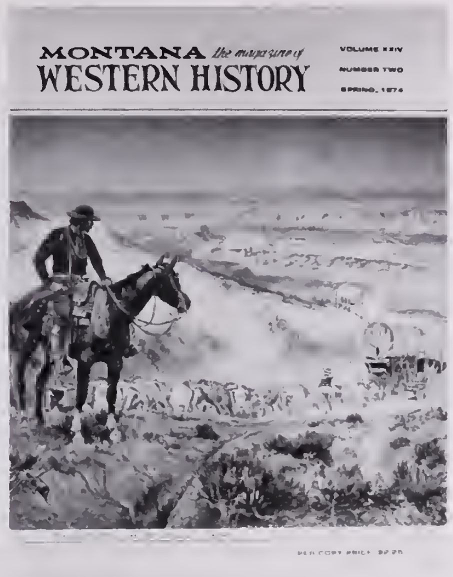

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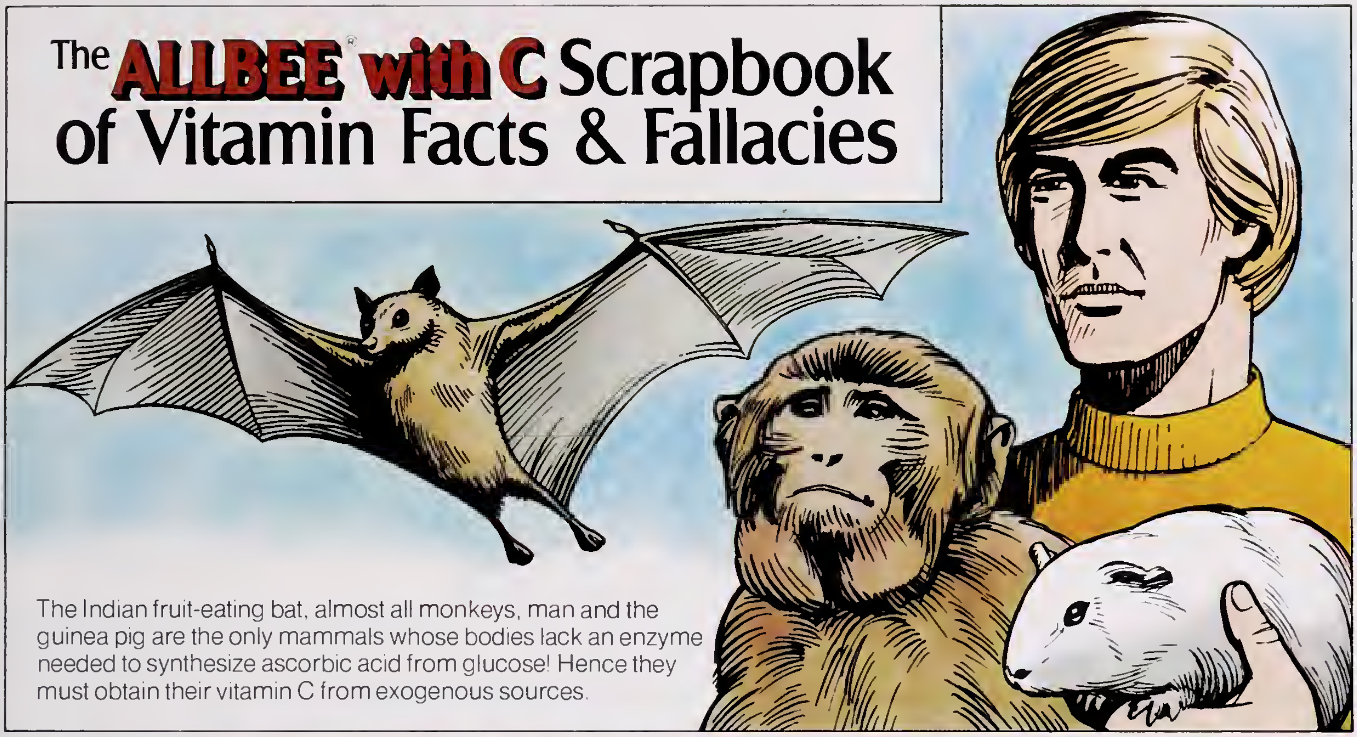
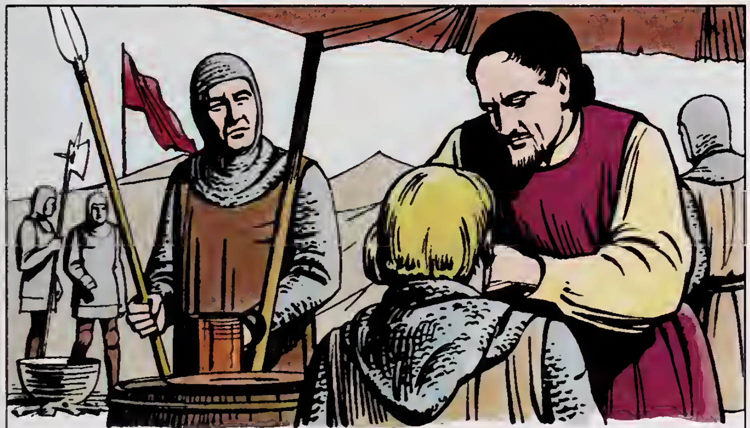
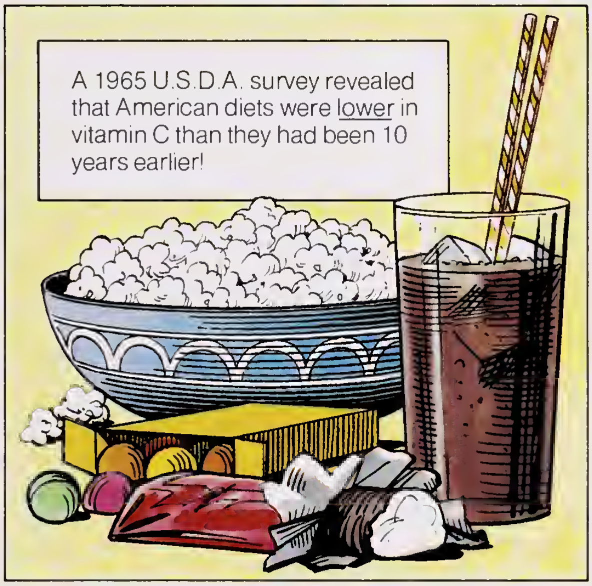


The Indian fruit-eating bat, almost all monkeys, man and the guinea pig are the only mammals whose bodies lack an enzyme needed to synthesize ascorbic acid from glucose! Hence they must obtain their vitamin C from exogenous sources.



De Joinville writing about a 13th century crusade reported that barber surgeons had to "cut away the dead flesh from the gums to enable people to masticate their food." The disease he described was probably scurvy.



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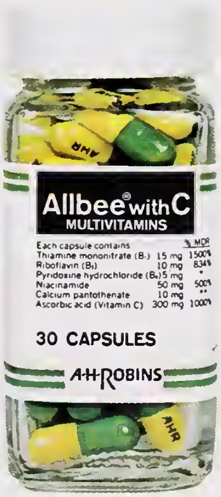
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President's Message*

What's wrong with America? I say nothing! What's wrong with the American Medical Association? I say nothing! What's wrong with the Montana Medical Association? I say nothing! What's wrong with the County Societies? I say nothing! What's wrong with physicians? I say non-participation!

Physicians today are losing their perspective about the profession, not through their own inadequacies but by abdication of personal pride and honor in being a physician! We, yes we, have destroyed ourselves by paranoia. We, yes we, have gone along with the negatives, which have been so overblown and so magnified, so incessantly discussed by others, that we have forgotten to communicate what's right with organized medicine among ourselves. Somewhere within us seems to be the need for Machiavellianism. Somewhere within us we have faltered in our confidence and in our decision making. Somewhere within us we have forgotten who we are and how we ought to act. We produce pale shadows of our actual capabilities.

What will energize the medical profession? Only confidence and leadership. You don't get it from those around you or from your leaders. You only find it within yourselves. We must all tap our reserves of stamina, resourcefulness, and common sense. There is a problem larger than our profession called "medical care for our people". Perhaps it seems insurmountable, leading some within our Association to urge that it be abdicated to those who pontificate "it shall be cured by legislation". I don't believe it. I believe that the most honored profession should and will guide our legislators to a mutually beneficial solution to the health needs of our nation, but only through cohesive efforts on the part of all of us.

My message tonight, now, not at some future period, *is* that organized medicine is right for America and for all of us. We are moving, changing, building, and accomplishing for the better on the boldest and most controversial issues of our existence—but we must do it together. It is not enough to rely on a few leaders elected or otherwise. We must expand our own thinking. But we must lead! That's what physicians ought to be best at—showing the way with actions, not conversation. Unfortunately, in the past, we have left the real thinking, the decision making too long to too many others—out of our own passivity. It is the time to become aggressive and to exert leadership.

There is nothing wrong with our profession. We are the most respected and honored of all—but let us believe it ourselves.

John R. Halseth, MD, President,
Montana Medical Association

---

* Presented at the Interim Meeting of Montana Medical Association, April 12, 1975.

Medicare and Diagnosis

Every doctor knows that the practice of medicine daily becomes more complicated. Now Medicare has informed us that there must be a diagnosis to support each test done on the patient. On the surface, this is a reasonable bureaucratic request—and usually not too difficult. "Congestive heart failure" (427.0) or "Acute bronchitis" (466) will support a chest x-ray. Even "Chest wall pain" (355.1) will support an electrocardiogram. But what does one do with the T4 on the somewhat pudgy Greek lady who never learned to speak English? Or what is an on-the-spot diagnosis for the late Friday "drop in emergency" with a fourteen year history which makes MacBryde's "Signs and Symptoms" look like a condensed version?

We have a colleague who uses "Possible internal disease" (796.9) for a Pap smear, but this seems a bit elusive and makes the patient more uneasy than the procedure. Maybe one could confuse the clerk in the Medicare office by using some of those diagnoses they've never seen before, like "Sucked into a jet" (E844) or "Healthy person accompanying sick relative" (Y08). Perhaps on some Saturday afternoon if one went through the whole book one could compile a quick reference list of a few medical entities which could support most common laboratory tests.

In the long run it would be better to be honest, but I can't find the correct diagnosis in the I.C.D.A. The book does not list "Muddled thinking", "Diagnostic hunch which didn't pan out", "Bum steer", "Red herring", or "Diagnostic dilemma". Does anyone know how you go about getting new diagnoses in the book?

G. A. Diettert, MD
Missoula

"Perioperative Antibiotics"

THE USE AND ABUSE of antibiotics has received considerable recent attention in both medical and lay writings. These powerful drugs have been responsible for the virtual elimination of some bacterial diseases, for a marked reduction in incidence of others, for an amelioration of sequelae in still others, and in many instances for effective and rapid treatment of established bacterial disease. Their proper use is predicated upon isolation of the offending bacteria, antibiotic sensitivity testing, and selection of the most effective antibiotic in proper dosage for the clinical condition.

Unfortunately, the widespread use of antibiotics has not always been in accord with these principles, and often they have been given hopefully and empirically to either treat established disease or to prevent bacterial disease from becoming established as a clinical infection. The relatively high incidence of allergic and toxic side effects coincident with the use of antibiotics is well known. Further, the propensity of bacteria to develop resistance to various antibiotics is also well established. The indiscriminate use of antimicrobial agents may conceivably select one or more strains of bacteria which are resistant to all antimicrobial agents.

The question then arises whether an antibiotic, or group of antibiotics, should be given to surgical patients in an effort to prevent wound infection. The establishment of clinical wound infection is dependent upon numerous factors such as host resistance, type of surgery, size of bacterial innoculum, virulence of innoculated bacteria, presence of dead tissue and presence of foreign bodies. A number of studies in the 1950's and early 1960's concluded that use of parenteral antibiotics not only did not reduce the rate of postoperative infection but, in fact, were associated with an increased incidence of infection in some studies. However, antibiotics were administered well after the surgical procedure in a preponderance of cases. More recently, studies from the fields of general surgery, gynecological surgery, and orthopedic surgery have unequivocally demonstrated the value of parenteral antibiotics in reducing the rate of postoperative wound infection in both clean and contaminated wounds when the following conditions were met:

1. The antibiotic was administered parenterally.
2. The antibiotic was administered perioperatively, i.e., just before, during, and immediately after the procedure.
3. The antibiotic was bacteriocidal and usually broad spectrum.

The sine que non in the prevention of postoperative sepsis is bacteriocidal tissue concentrations at the operative site at the time of surgery.

Since deep surgical wound infection continues to occur, causing a significant morbidity (and even mortality), prolonged hospitalization, and lost time from work, and costing ever increasing sums of money for treatment, the reduction of deep surgical wound infection is desirable. In addition to strict adherence to traditional surgical and aseptic technics, it would appear both reasonable and desirable to advocate the proper use of perioperative antimicrobials in surgical patients who have decreased host defenses (diabetes, cortisonism, immuno-suppressives or inherited or acquired impairment of anti-bacterial systems), who undergo prolonged and extensive surgery, or who have surgery involving implantation of large amounts of foreign materials.

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Pseudomembranous colitis associated with clindamycin therapy

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PSEUDOMEMBRANOUS COLITIS is an uncommon complication of antibiotic therapy.[1-5] Three cases of severe colitis with proctoscopic and roentgenographic findings consistent with pseudomembranous colitis occurred in one hospital over a two month period. All had received clindamycin for presumed respiratory tract infections.

CASE REPORTS

Case 1: A 61-year-old male with a history of previous stroke underwent bilateral Caldwell-Luc operations for severe right facial pain due to chronic sinusitis. One day after surgery, he had a temperature of 102° and was started on clindamycin 150 mg. by mouth four times daily. Three days after starting clindamycin, he had four loose watery bowel movements. He continued to take the clindamycin for 12 days and his diarrhea became more severe. He was readmitted with signs of dehydration and was having at least 20 loose watery bowel movements per day. Physical examination showed an elderly male with moderate dehydration and postural hypotension. The temperature was 98°. The abdomen was not distended, and no masses or tenderness were elicited. He had decreased movement of the palate on the right as well as right-sided hemiparesis. Proctoscopy showed edematous and friable mucosa with thick patches of gray-white exudate adherent to the mucosa.

Cultures of the stool disclosed no pathogenic bacteria or parasites. Barium enema x-rays showed massively enlarged and edematous folds with questionable shallow ulcerations. Small bowel x-rays showed mild edema of the mucosa.

On admission, the patient was fed cultured buttermilk and lactobacillus granules with no improvement in his symptoms. After one week, prednisone 60 mg. by mouth was begun with some clinical improvement but was discontinued after five days when x-rays showed osteomyelitis adjacent to the right frontal sinus. Because of repeated pulmonary aspiration of various types of oral feedings over the next two weeks, intravenous hyperalimentation with casein hydrolysate and dextrose was begun and the patient rapidly improved over ten days. Repeat proctoscopic and roentgenographic examinations showed complete resolution.

Case 2: A 50-year-old female with known metastatic carcinoma of the breast and pseudomucinous cystadenoma of the ovary had a partial small bowel resection for obstruction secondary to tumor. Postoperatively she developed pneumonia and subsequent respiratory failure requiring tracheostomy and intensive respiratory assistance. She received clindamycin 600 mg. I.V. q 6 hrs. for 16 days. She also received cephalothin 7 mg. intramuscularly every six hours for four days and gentamycin 50 mg. I.V. every six hours for five days during that time.

On the day the clindamycin was discontinued she developed loose watery diarrhea which increased to 10 to 15 stools per day over the next several days. The diarrhea did not respond to diphenoxylate with atropine, lactobacillus granules, or tincture of opium. A barium enema showed marked edema of the sigmoid and rectal mucosa with ulceration (Fig. 1). A proctosigmoidoscopy the following day showed edematous, friable rectal mucosa covered with fibrinous exudate. Smears of rectal secretions showed multiple organisms, and cultures disclosed no pathogenic bacteria or parasites.

She received enemas of homogenized feces donated by a healthy physician twice daily for three days and low residue protein hydrolysate feedings. Over two weeks her diarrhea gradually disappeared.

Case 3: An 80-year-old female was initially hospitalized for six days for severe pharyngitis, malaise, and fever. She was treated with intramuscular cephaloglycin and oral clindamycin 150 mg. four times daily with good response of her symptoms. The day following discharge, she developed five loose watery bowel movements and was readmitted to her local hospital. There over the nine days her diarrhea was severe enough to require intravenous fluid therapy for dehydration. A barium enema x-ray showed diffuse mucosal ulceration and edema through the entire colon. Intravenous hydrocortisone and oral salicylasosulfapyridine were begun. Over the next three days she developed abdominal distention and became hypotensive despite three to four liters of intravenous fluid replacement. Cephalothin 1 gm. intravenously four times daily and streptomycin 500 mg. intramuscularly twice daily were begun. On the third day, the patient had no recordable blood pressure and was unresponsive and was transferred to the University hospital.

Physical examination showed a cyanotic unresponsive female. Her blood pressure could not be recorded. The pulse was 140/min. Her abdomen was markedly distended with some shifting dullness. There was no peripheral edema. Proctosigmoidoscopy disclosed edematous, friable mucosa with an adherent fibrinous exudate. x-rays of the abdomen showed diffusely enlarged colon with mucosal irregularity consistent with edema throughout the entire colon. Laboratory studies after considerable intravenous fluid had been given showed a hemoglobin of 12.0 gms. percent and a white blood count of 12,400 with 80 neutrophils, 2 myelocytes, 1 promyelocyte, 15 lymphocytes and 3 monocytes. The platelet count was 14,000 per ml. The prothrombin time was 22 seconds, partial thromboplastin time was greater than 180 seconds, and factor V was 15 percent. The creatinine was 2.5 mg. percent, serum glutamic oxalacetic transaminase 840, alkaline phosphatase 136 international units, and bilirubin was 1.1 mg. percent. Stool cultures were negative for pathogenic bacteria or parasites.

The patient was treated with large quantities of intravenous saline, plasma, and whole blood. As her blood pressure rose to normal levels, she became responsive and alert. Intravenous heparin and fresh whole blood were administered for 20 hours because of clinical and laboratory evidence of disseminated intravascular coagulation. She was also treated with ACTH 40 units intravenously every 8 hours. After the first 24 hours in the hospital, the patient remained stable for the next four days, and then had a temperature of 101°, and blood cultures grew alphastreptococcus. Gentamycin intravenously was begun and the patient became afebrile. She again remained clinically stable with three or four loose bowel movements per day for six days. X-rays of her abdomen showed little change from admission except for some increase in ascites. Her serum bilirubin climbed to a total of 8.9 mg. percent with a direct-reacting fraction of 3.9 mg. percent. On the eleventh day, she had a temperature of 102° with blood cultures that later grew *Pseudomonas aeruginosa*. She was given kanamycin and cephalothin, but she became hypotensive and unresponsive to any therapy and expired.

Discussion

Pseudomembranous enterocolitis is a poorly understood inflammatory disease of the gut, characterized by the formation of membranous-like collections of exudate over the underlying mucosa. In the past it has been associated with many diverse entities, including postoperative bowel surgery, uremia, congestive heart failure, and ischemia of the gut. Bacterial infection or endotoxin damage, particularly due to staphylococcus aureus, have been incriminated as an etiological agent in enterocolitis.[1] However, the recovery of this agent in enterocolitis is inconsistent, and patients frequently have diarrhea with staphylococcus aureus isolated but no evidence of mucosal damage.

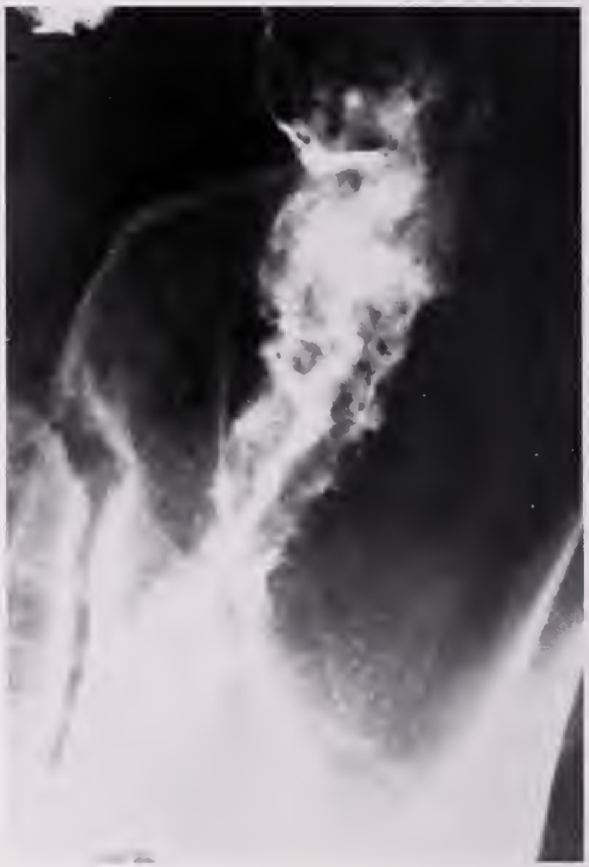

Fig. 1. Marked edema of the sigmoid and rectal mucosa with ulceration are shown.

Most recently psuedomembranous enterocolitis has been reported following use of various antibiotics, including ampicillin,[2] penicillin,[1] chloramphenicol,[3] erythromycin,[1] lincomycin,[4] neomycin,[1] and tetracycline.[3] It has been postulated that in some patients the growth of resistant organisms causing inflammation and exudate is the cause of the disease. Acceptance of this theory is precluded by the lack of microbial confirmation of pathogenic organisms and by the fact that enterocolitis was well established prior to the advent of antibiotics. However, many cases of enterocolitis occur in otherwise healthy individuals after the use of antibiotics despite the absence of underlying disease.

As many as fifty percent of patients receiving oral lincomycin developed diarrhea while taking the drug. Some patients developed inflammatory changes indistinguishable from ulcerative colitis and three cases of pseudomembranous enterocolitis have been confirmed.[4,5] Clindamycin is a synthetic modification of lincomycin that supposedly had fewer gastrointestinal side effects. Most preclinical trials of clindamycin reported a low incidence of diarrhea, although one-third had an increase in loose stools during the trials.[6] Clindamycin was initially marketed as the drug of choice for antibiotic therapy in anaerobic infections.[7] Its use was also postulated in certain respiratory infections in penicillin-sensitive patients. Within the last year there have been reports of pseudomembranous enterocolitis occurring in increasing frequency.[8] This suggests that its incidence is more common than had been previously suspected.

Prior to these cases reported there had been only one other identifiable case of pseudomembranous enterocolitis in our hospital in the previous three years, and that was due to lincomycin. Since these cases occurred within a few months after clindamycin had been licensed for clinical use, it is likely that they represent a growing incidence of this complication.

A recent review of over two hundred consecutive patients given oral or parenteral clindamycin revealed an incidence of diarrhea in twenty per cent of the patients and pseudomembranous enterocolitis in ten per cent of the patients.[9] Since pseudomembranous enterocolitis carries a mortality of approximately twenty percent, the use of this antibiotic should be restricted to documented infections of anaerobic bacteria. This complication also represents the need for reporting of adverse effects of all drugs by physicians.

Summary

Three adult patients who received clindamycin for respiratory tract infections developed severe diarrhea with proctoscopic and roentgenographic findings consistent with pseudomembranous colitis. One patient died of complications of the disease and the other two recovered after a prolonged illness. There was no evidence for infection with *Staphylococcus aureus* or other pathogenic bacteria. Since these three cases occurred within a few months after clindamycin became available in a hospital where only one case had been reported in the preceding three years, pseudomembranous colitis may be a more common complication of the use of clindamycin than previous reports suggest.

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Hazards of combination therapy of hypertension*

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INITIAL COMBINATION DRUG THERAPY of hypertension has had widespread use over the last few years. In the past year some, but not all, manufacturers of hypertensive drugs have prudently advised that the fixed combination of drugs is not indicated for therapy of hypertension without prior titration of the individual drugs. An important statement by Freis of Georgetown University bears repetition: "complete sympathetic blockade is not essential to obtain adequate blood pressure control."[1]

CASE REPORT

A 194-pound hypertensive female without cardiac failure was initially treated with 750 mg. of methyldopa per day for several weeks without apparent benefit. She was then changed without titration to one Salutensin tablet (hydroflumethiazide 50 mg./reserpine 0.125 mg.) and one Ismelin tablet (guanethidine 10 mg.) each morning for about eight months. During at least the last five months she stated she had symptoms of extreme exhaustion, especially in the morning, suggesting moderate sympathetic blockade.

During the second week of February 1974, she developed a flu syndrome with fever and vomiting. Marked sympathetic blockade occurred with dizziness and weakness when in any degree of the upright position accompanied by bradycardia with heart rate of 42 and with orthostatic hypotension of 72/60. All drugs were stopped. ST and T wave changes increased on the electrocardiogram with beginning ambulation. Repeated cardiac enzymes were normal. All of these symptoms and signs gradually reversed over a six week period. A treadmill test was then essentially normal. A creatinine clearance test was 48 ml./min. A plasma renin level taken at the end of four hours in the supine position was low normal at .13 ng./ml./hr. suggesting to some that the diuretic or an aldosterone antagonist might be expected to give the best control.[2] The blood pressure had resumed the former high level of 190/110 after six weeks without drugs.

She felt much better over the six months from April 2 to August 9, 1974, when her weight decreased from 179 pounds to 162 pounds, although a low blood pressure and symptoms of headache and dizziness were frequently recorded. A daily dose of 100 mg. of Hygroton was restarted and was gradually lowered to 25 mg. every other day with recurrence of continued dizziness and lower blood pressure especially with any five pound weight loss. She best tolerated hydrochlorothiazide 25 mg. daily, but on one occasion also had low blood pressure and dizziness with this amount of drug, again during a period of weight loss. The medication was stopped and the blood pressure rose to a previous high level. Hydrochlorothiazide was resumed, and with no further weight loss the blood pressure has been controlled without dizziness or excessively low blood pressure. After resumed treatment, inverted T wave changes recurred on the electrocardiogram and have remained unchanged.

Discussion

The metabolism of the three drugs used in combination was reviewed extensively, and space does not permit complete discussion of each. Review of the literature regarding reserpine is the most rewarding because the early noted fact that reserpine appears to be stored in animal fat tissue is completely by-passed in discussions in the later literature.

In 1957 A. J. Plummer et al reported on the metabolism of reserpine.[3] They pointed out that reserpine, an alkaloid discovered in Rauwolfia Serpentina in 1952 by Mueller, exerts a prolonged hypotensive and quieting influence. Brodie had established that the serotonin content of various tissues, including brain, was reduced by reserpine and Holzbauer and Vogt also observed that reserpine affected a lowering of the norepinephrine content of the brain. Plummer's group attempted to employ more sensitive analytical technics. In vivo experiments in guinea pigs with reserpine labeled with 14C (in the 4-methoxy group of the 3, 4, 5, trimethoxybenzoate moiety) showed that the maximum concentration of 14C was reached within an hour of injection, and fell to comparatively low levels within six hours in all organs studied, with the exception of fat. Fat tissue was unique in slowly accumulating 14C, which reached a maximum in four hours and was still detectable in significant concentration after 24 hours. Fat and liver were the only tissues in which 14C could be found actively after 24 hours and only in Fraction B (reserpine factor).

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Plummer et al then conducted experiments in rats with reserpine labeled with 14C (in the carboxyl carbon of 3, 4, 5 trimethoxybenzoate). As previously noted, the levels of Fraction B (reserpine like) in fat were persistently elevated. Chromotography on silica gel showed that the substance in the fat depot had the characteristics of reserpine. Very little of 14C of Fraction B (reserpine like) was found in the urine or feces of either species. From similar studies with reserpine labeled with tritium they concluded that the rate of uptake of reserpine by brain does not differ significantly from that of all other tissues except fat.

Observations which demonstrate this fat storage of reserpine in humans appear in a study of excretion and metabolism of reserpine in renal failure by Zsote'r and associates from the University of Toronto in 1973.[4] They studied 15 patients with some renal failure to determine the metabolism and excretion of reserpine, using one intramuscular injection of H-reserpine labeled with tritium. Twenty-four hour creatinine clearance tests were used to determine renal function before and after reserpine administration. The age, weight in kilograms, height in centimeters, and height to weight ratios were determined as well as the plasma half-life of reserpine in hours. The creatinine clearance varied from 1.4 ml/min. to 92.9 ml/min. and was 85 ml/min. in their most obese patient. Their patients with creatinine clearances above 50 ml/min. excreted more non metabolized reserpine and the plasma levels of radioactivity showed an initial phase of relatively rapid decline during the first 12 to 24 hours after injection followed by a much slower fall in subsequent days. Increase in the plasma half-life was obvious only in patients with a creatinine clearance lower than 10 ml/min. Over 10 ml/min. the time was 45 to 80 hours. Under 10 ml/min. it ranged from 87 to 323 hours. The only exception to this was their most obese subject with the very normal creatinine clearance who excreted considerably less radioactivity in the urine and had a plasma half-life of 162 hours. They stated that obesity may be a factor influencing the renal elimination of reserpine. They concluded further that their patients with the longer half-life demonstrated no increase in the pharmacologic effects of reserpine being likely explained by the extensive metabolism of the drug. Plasma levels were in most patients undetectable after 24 hours although almost 50 percent of the injected reserpine remained in the body beyond the 7 day collection. They quoted Numerof and associates as reporting radioactivity in the blood 6 weeks after oral 14C reserpine and concluded that the extensive storage of the drug could be a factor minimizing the consequences of renal failure. Numerof et al[5] also reported that their most obese patient appeared to have reserpine blood levels higher than those of their other patients, and maintained longer at a high level than the other patients. They said "Shepperd has shown that in rats, reserpine is deposited in fat, and the same condition may exist in man also."

It would appear from these studies that reserpine taken orally day after day can be stored in some manner in large quantities in the fat tissue of the body. It also seems logical to postulate that weight loss with some type of break down of fat tissue or metabolic activity could release reserpine or a stored reserpine factor with some pharmacologic activity in unpredictable amounts to participate in an antihypertensive role in combination with other agents being taken orally. This postulation would explain why the blood pressure of our obese patient was so difficult to properly control over the last six months.

Guanethidine is stored mainly in the kidney, heart and blood vessel tissue.[6] Freis said Maxwell and Dollery have indicated that there is a prolonged action and slow excretion of guanethidine even with one dose daily and a cumulative effect will be obtained over a period of 5 to 7 days.[1] The range of effective dose of guanethidine has varied from as little as 5 mg. up to 500 mg. per day and each patient must be titrated. Reserpine depletes noradrenalin from both of its known pools.[7] Guanethidine is believed to directly block the adrenergic impulse and partially deplete the noradrenalin from only one of its two known pools, the stored pool. One sympathetic blockade effect is dilatation of the arterial and venous circulation with venous pooling creating a relative plasma volume reduction and hypotension.[1]

The thiazide drugs cause sodium depletion, reduction of extra-cellular fluid, and a true volume reduction of the plasma, in addition to a direct reduction of a peripheral resistance in the arteriole creating further hypotension.[8] Maximum blood pressure lowering in patients receiving oral diuretics is achieved in 3 to 4 weeks according to L. B. Page.[9] Vomiting and fever also reduce plasma volume and add to the hypotension.[1]

The depletion of cardiac cathecholamines by guanethidine and reserpine, is thought to remove a potentially important mechanism for augmenting myocardial contraction, and complete blockade allows parasympathetic stimulation to be unopposed and bradycardia can occur.[10] Poor coronary perfusion can follow. As this patient very gradually increased activity augmented myocardial contraction was probably needed. With the complete ganglionic blockade ST and T wave changes increased without evidence of myocardial infarction as indicated by repeated normal cardiac enzymes and gradually returned to normal as the heart rate and blood pressure returned to values prior to treatment. With further treatment and weight loss the T wave inversion returned and has remained without certain explanation.

In our review of the literature only one paper discussed the combination of guanethidine and reserpine in treatment. In 1973 Guazzi et al said "in our experience we have been surprised by the occurrence of heart failure during

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guanethidine and reserpine administration in hypertensive patients with no history or clinical symptoms of circulatory decompensation as regards the mechanism by which failure was induced." They suggested reserpine and guanethidine could depress cardiac performance either by interrupting the sympathetic drive to the heart, or by promoting fluid retention or both. A diuretic or a diuretic plus digoxin relieved the decompensation in their patients. To our knowledge, each drug alone has not been involved in causing frequent cardiac failure, but the combination undoubtedly causes a more complete sympathetic blockade.

Summary

It would appear that small daily doses of guanethidine and reserpine can accumulate in the body over a period of time and create too complete a sympathetic blockade, and some of the effects of blockade are increased by thiazide.

Since guanethidine, and especially reserpine, are very slowly removed from the body, the reversal of untoward effects takes a number of weeks and perhaps months and can cause untold problems in clinical management.

Therefore careful titration of individual drugs is advisable before any combination is considered. A combination of thiazide, reserpine, and guanethidine is contraindicated initially without titration of the individual drugs and should probably be used with caution at any time.

Reserpine because of its probable storage in fat tissue should be avoided in the obese patient.

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Ureteral reflux in infancy*

Relation to pyelonephritic scarring in adults

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THE RELATIONSHIP BETWEEN URETERAL REFLUX and chronic pyelonephritis was first suggested in 1903 by Sampson, who noted that vesicoureteral reflux was a "factor associated with some cases of pyelonephritis."[1] However, it was not until 1960 that Hodson and Edwards demonstrated that renal damage resulting from ureteral reflux was radiographically indistinguishable from chronic pyelonephritis.[2] Since then, many authors have noted and documented the association of chronic pyelonephritis and vesicoureteral reflux.[3-6]

In 1970, Rolleston, Shannon, and Utley[7] reported 175 infants under one year of age with documented urinary infection. These patients were evaluated with voiding cystograms and intravenous pyelograms. Forty-nine percent were demonstrated to have ureteral reflux. The reflux was graded into three categories: slight, if reflux could be demonstrated to enter the ureter only; moderate, if reflux entered the renal pelvis but did not distend the renal pelvis or ureter; and gross, if reflux caused dilatation of the ureter and/or renal pelvis and calyces. No infant underwent surgery for reflux. In those children with demonstrated reflux, 24 ureters (19 percent) had slight reflux, 74 ureters (57 percent) had moderate reflux, and 32 (25 percent) had gross reflux. It is of note that in all but three patients, initial renal scarring was associated only with gross reflux. Furthermore, only in ureters with gross reflux could progressive renal damage be demonstrated on urograms. (Fig. 1) Subsequent long-term followup of 58 patients with moderate ureteral reflux treated conservatively has demonstrated only one case of progressive renal scarring.[8] This data has led these investigators to conclude that, although all patients with ureteral reflux need careful followup care, only patients with gross reflux are at significant risk in terms of developing pyelonephritic scarring, and only these infants need be treated surgically. Those children with slight or moderate reflux were believed to be not at sufficient risk to warrant surgery.

As a result of their followup studies, Rolleston and associates also noted a strong tendency for spontaneous cessation of reflux over a period of years. Even in patients with gross ureteral reflux there was a tendency for the reflux to become of lesser degree. In other published reports, the incidence of reflux associated with renal damage has been considerably higher in children than in adults. This has suggested to many authors that some form of "maturation" of the ureterovesical junction has occurred, causing reflux to stop, but leaving many patients with severe renal scarring. This belief has been strengthened by the observation that similar renal scarring in adults rarely occurs in the absence of reflux, even in the presence of acute pyelonephritis.[5]

In 1969, Lyon, Marshall, and Tanagho were able to demonstrate a correlation between the incidence of reflux and the configuration and position of the ureteral orifice.[9] From the data obtained from their study, they were able to predict the probability of reflux occurring through a given ureteral orifice on the basis of their cystoscopic findings alone. On the basis of these observations, we postulated that if the renal scarring found in adults were due to previous reflux, similar changes in the ureteral

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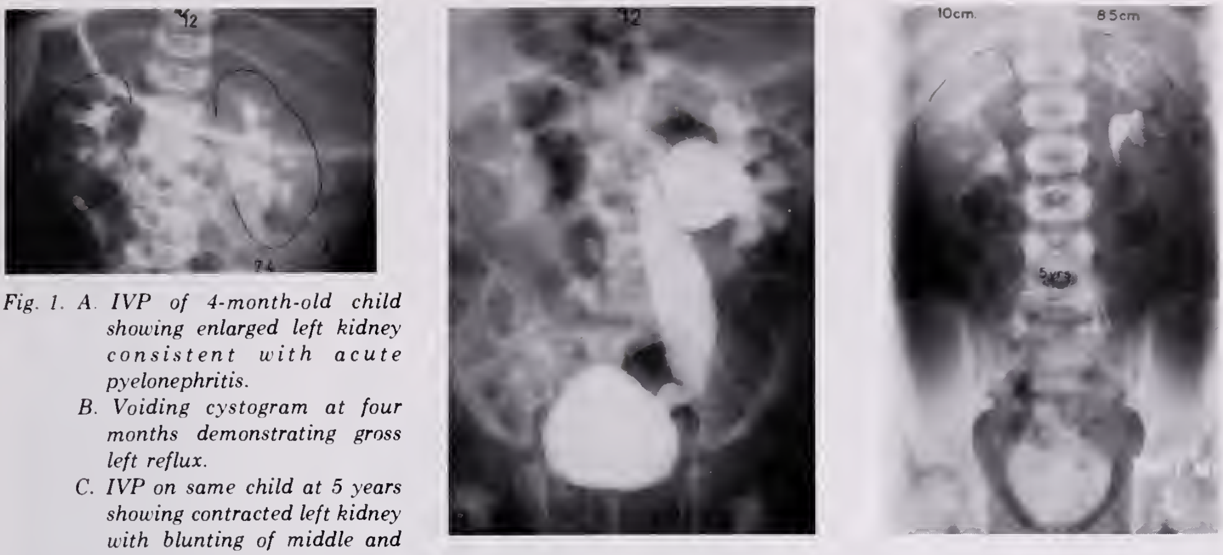

Fig. 1. A. IVP of 4-month-old child showing enlarged left kidney consistent with acute pyelonephritis.
B. Voiding cystogram at four months demonstrating gross left reflux.
C. IVP on same child at 5 years showing contracted left kidney with blunting of middle and lower pole calyces.

orifice should still be reflected in the ureteral orifices of these patients, even though reflux could no longer be demonstrated. A study was, therefore, undertaken to ascertain the appearance of the ureteral orifices in an unselected group of adult patients with chronic pyelonephritis.

Study

Since 1958, all patients with chronic nonobstructive pyelonephritis demonstrated on intravenous urograms have been recorded at Christchurch Hospital. Chronic pyelonephritis was defined as radiographic demonstration of local or generalized parenchymal thinning with scarring of the associated calyx or calyces. (Fig. 2) All patients in this study were initially evaluated with an IVP and voiding cystourethrogram. Any patient with upper or lower urinary tract obstruction, calculous disease, or a history of analgesic abuse was excluded from the study.

In 1970, at the time of this study, 106 of these patients were over the age of 12, and during that year many of these patients were re-admitted to Christchurch Hospital because of decreasing renal function, recurrent urinary infections, or for surgical assessment. Sixty-seven of these underwent cystoscopic examinations. Of the remaining 39 patients who did not have cystoscopy, 16 had already died from renal failure and 23 were either lost to followup or their medical condition was felt to contraindicate the procedure.

At the time of cystoscopy, all ureteral orifices were classified by the system described by Lyon et al.[9] These authors assigned ureteral orifices to one of 4 groups depending on their cystoscopic appearance: a normal orifice was designated a grade 0, a ureteral orifice resembling a football stadium was designated grade 1, orifices that had lost their medial attachments to the trigone and were horseshoe shaped were grade 2, and those orifices with a golfhole appearance were classified as grade 3 and were the most abnormal. The position of the ureteral orifices was also evaluated. Orifices in a normal medial position on a well-developed trigone were in position A; if the orifice was located far posterolaterally, and not attached to any identifiable trigone, it was in position C. Position B was midway between the other two positions and had minimal trigonal attachments.

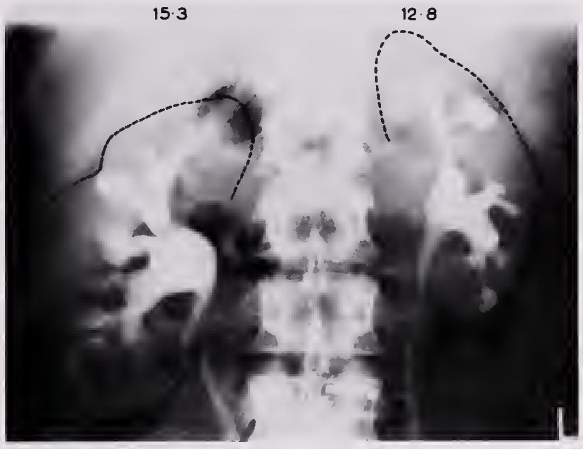

Fig. 2. 33-year-old female with 8-year history of urinary infections. IVP shows diffuse loss of parenchyma on left with calyceal scarring. There is loss of parenchyma over right middle calyx.

Lateral Position	Orifice Grade 0	Orifice Grade 1	Orifice Grade 2	Orifice Grade 3
A	0% 0/13	0% 0/4	100% 1/1	0%
B	22% 2/9	26% 5/19	31% 11/36	100% 4/4
C	0% 0/1	0% 0/4	47% 14/30	77% 10/13

0 NO. REFLUXING / 0 NO. ORIFICES

Fig. 3. Incidence of ureteral reflux related to grade and position of ureteral orifice.

Lateral Position	Orifice Grade 0	Orifice Grade 1	Orifice Grade 2	Orifice Grade 3
A	46% 6/13	25% 1/4	100% 1/1	0%
B	55% 5/9	68% 13/19	70% 25/36	100% 4/4
C	100% 1/1	100% 4/4	80% 24/30	100% 13/13

0 NO. SCARS / 0 NO. ORIFICES

Fig. 4. Incidence of renal scarring related to grade and position of ureteral orifice.

Results

The position and configuration of the ureteral orifices were evaluated in this study group of 67 patients. Of these 134 ureteral orifices, 97 were associated with chronic pyelonephritic scarring. There were 47 ureteral orifices with reflux and only two of these were not associated with renal scarring.

The distribution of the ureteral orifices related to position and configuration and the incidence of associated ureteral reflux is shown in Fig. 3. This figure demonstrates that, as the ureteral orifice becomes more abnormal in position and configuration, the incidence of reflux through these orifices increases. Of the 45 scarred kidneys associated with reflux, all were found to have orifices that were abnormal, although three of these were not abnormal in both position and configuration.

The incidence of chronic pyelonephritic scarring in relation to the position and configuration of the ureteral orifices is shown in Fig. 4. It is apparent that the incidence of renal scarring increases as the orifice becomes more abnormal. Of the 45 scarred kidneys associated with reflux, only three were normal in either position or configuration. Of the 52 scarred kidneys not associated with reflux, 46 (88 percent) were associated with ureteral orifices that were abnormal in position or configuration and 41 (79 percent) were associated with orifices that were abnormal in both respects. Only six kidneys with pyelonephritic scarring were associated with completely normal (position A, grade O) orifices. In one kidney with a nearly normal orifice, (position A, grade 1), a renal scar developed during the period of study in the absence of reflux. The details on these patients with normal or nearly normal orifices have been previously published.[11]

Discussion:

Since 1960, vesicoureteral reflux has been found in increasing numbers of patients with chronic pyelonephritis. In some studies, ureteral reflux has been demonstrated in up to 53 percent of infants and adults with chronic pyelonephritis.[11] Many investigators have noted also that, except in patients with neurogenic bladders, most chronic pyelonephritic scarring occurs quite early in life, that is, at a time when vesicoureteral reflux is most common.[11] Although renal scarring may be due to a variety of causes, we believe that this study, coupled with the work of Lyon and associates, suggests that vesicoureteral reflux is responsible for many pyelonephritic changes in patients with abnormalities of the ureteral orifice, even in the absence of proven reflux.

In a group of 330 girls, with recurrent urinary infections. Lyon and associates demonstrated that patients with demonstrable vesicoureteral reflux could be fairly accurately predicted at cystoscopy by evaluating the configuration and position of the ureteral orifices.[9] However, most authors would agree that the incidence of ureteral reflux is considerably lower in adults and that it probably persists only in those patients with severe trigonal anomalies. In

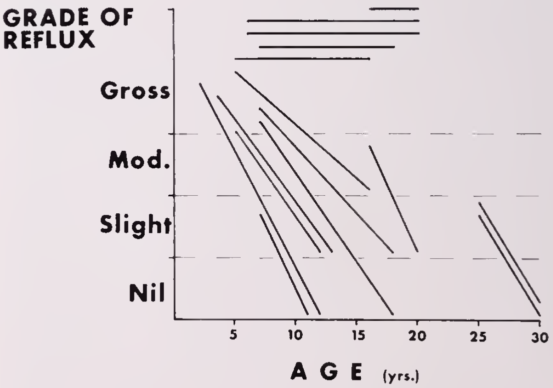

Fig. 5. Change in degree of reflux with age (each line represents one renal unit).

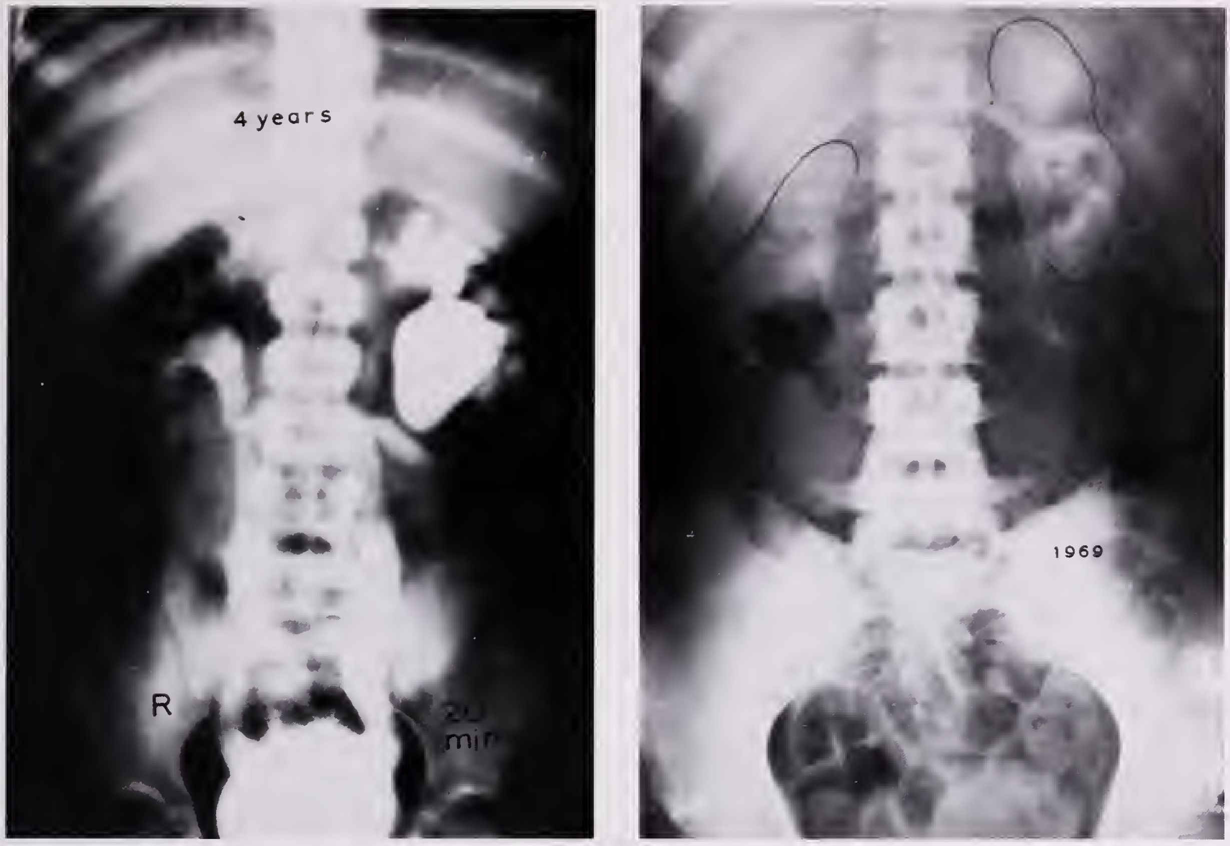

Fig. 6. A. Voiding cystogram of girl at age 4 demonstrating gross ureteral reflux.
B. IVP of same girl at age 17 shows extensive bilateral renal damage. No reflux was demonstrated at this time.

the remainder of patients, reflux ceases for unknown reasons. Hutch has suggested that the maturation and lengthening of the intravesical ureteral tunnel are largely responsible for the termination of reflux at puberty.[12] Others believe that spontaneous maturation seldom occurs.[13] However, if our premise that chronic pyelonephritis in adults is caused by ureteral reflux in infancy and childhood is correct, then some form of maturation of the ureterovesical junction must occur.

In our study, fifteen renal units were followed with serial cystourethrograms for five to fifteen years. (See Fig. 5.) Eleven of these fifteen ureters were associated with gross reflux and five of them demonstrated no change in the amount of reflux during the followup period. However, the remaining six ureters with gross reflux showed marked diminution in degree of reflux. In four of the latter the reflux became slight and in two of them it ceased altogether. This seems particularly significant since all of the ureters in which gross reflux diminished or terminated had grossly abnormal ureteral orifices that were located far posterolaterally (position C) and were either horseshoe shaped or golfhole in appearance (grade 2 or 3).

One patient graphically illustrated this sequence (Fig. 6). A 4-year-old girl when first seen had gross bilateral ureteral reflux. She was, thereafter, lost to followup for 13 years, at which time she was again seen with a urinary infection. At that presentation, she had blood pressure of 200/130, BUN was 90, and her IVP showed bilateral changes of chronic pyelonephritis. No ureteral reflux could be demonstrated at this time. At cystoscopy in 1970, the ureteral orifices were located far posterolaterally and were golfhole in appearance (position C, grade 3). This case history suggests, at least anecdotally, that even very abnormal orifices can stop refluxing. It also suggests the plausibility that chronic pyelonephritis in the adult may be due to previous reflux, which has stopped.

Summary

Previously published work from Christchurch Hospital has suggested that ureteral reflux is very common in infants with urinary infections. However, their data suggests that only those children with gross reflux are at risk in terms of presenting initially with pyelonephritic scarring and these children are nearly the only patients who go on to develop more scarring.

Since the renal damage resulting from ureteral reflux is radiographically indistinguishable from chronic non-obstructive pyelonephritis, a study to ascertain the etiology of radiographic pyelonephritic scarring in a group of adult patients was carried out. Since 1958, 106 patients, all over 12 years old, have been seen with chronic non-obstructive pyelonephritis at Christchurch Hospital. Cystoscopy was carried out in 67 of these. Of these 134 ureteral orifices evaluated, 97 were associated with pyelonephritic scarring, and 45 had demonstrable vesicoureteral reflux. All refluxing orifices were abnormal. Of ureteral orifices associated with renal scarring but no demonstrable reflux, 79 per cent (41/52) were found to have abnormalities of such degree that ureteral reflux seems likely to have occurred in the past.

This data suggests that, overall, 89 per cent (86/97) of the pyelonephritic scars found in this study are the end result of vesicoureteral reflux or changes initiated by reflux during infancy and childhood (Fig. 7).

SUMMARY

Ureteral orifices examined	-134
Kidneys with parenchymal scarring	-97
A. Renal scarring with reflux	-45
Abnormal orifices	-45 (100%)
B. Renal scarring without reflux	-52
Abnormal orifices	-41 (79%)
Overall incidence of abnormal orifices in kidneys with scarring	-89% (86/97)

Fig. 7. Summary of study data.

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Concomitant aortic aneurysm and horseshoe kidney*

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The authors present a case report of this entity, a collective review of the cases in the English literature, and a discussion of current management.

ANOMALIES OF THE URINARY TRACT may present formidable obstacles in the management of abdominal aortic aneurysms. A recent encounter with the interesting and challenging association of an abdominal aortic aneurysm and a horseshoe kidney prompted this report and a review of the thirty-nine cases described in the English literature, which have been managed surgically.

CASE REPORT

A 62-year-old white male, tool and die designer, was admitted to the Milwaukee County Medical Complex with a three month history of epigastric and substernal pain associated with diaphoresis and dyspnea, relieved by nitroglycerine. He had been treated for hypertension and diabetes for several years. He was also aware of a pulsatile epigastric mass. A carotid arteriogram had been performed in another hospital, one year previously, for dizziness and vertigo. Mild left carotid stenosis was demonstrated. Instituted Coumadin therapy relieved his cerebrovascular symptoms.

Physical examination on admission confirmed a pulsatile mass in the epigastrium. Blood pressure was 160/90 and the pulse was 80 and regular.

Cardiac catheterization showed severe atherosclerotic coronary artery disease. An aortogram demonstrated a fusiform abdominal aortic aneurysm involving both common iliac arteries. (Fig. 1) The conformation of the renal pelves and ureters suggested the presence of a horseshoe kidney. Single right and left renal arteries were noted, but no aberrant vessels were seen. An excretory urogram clearly defined the renal outflow tracts and confirmed the suspicion of a horseshoe kidney (Fig. 2). BUN was normal.

Aorto-coronary vein graft to the left anterior descending artery was carried out under hypothermic cardiopulmonary bypass. The postoperative course was unremarkable except for the development of atrial flutter which responded to cardioversion.

Three weeks later, July 12, 1971, surgery for the abdominal aortic aneurysm was performed. The aneurysm measured seven centimeters in diameter and involved both common iliac arteries. Three renal vessels were identified. Two arose conventionally from the aorta above the aneurysm and supplied major portions of the two sides of the horseshoe kidney. A small, patent, branch arose from the lower portion of the aneurysm near the middle sacral artery. This vessel supplied the overlying isthmus of the horseshoe and a portion of the left side of the renal mass.

Vigorous diuresis was established by the administration of an additional liter of Ringer's lactate and the intravenous infusion of 12.5 grams of Mannitol. Heparin, 5,000 units, was injected into the aorta just proximal to the aneurysm, and the aorta was cross clamped below the two main renal arteries. The isthmus of the horseshoe kidney and the left lower polar portion became cyanotic and were sharply demarcated from the remainder of the renal mass, indicating the isolated dependence of this portion of the parenchyma on the isthmic artery. The aneurysm was resected by the endoaneurysmorrhaphy technic described by Creech.[6] A knitted dacron bifurcation prosthesis was interposed between the infrarenal aorta and the distal common iliac arteries.

The isthmic artery arising from the aneurysm was preserved with a cuff of the aneurysmal wall. This vessel was implanted into the left iliac limb of the dacron graft as a "button" patch. The cyanosis of the renal isthmus disappeared immediately with reperfusion of this artery. The postoperative course was uncomplicated. The blood urea nitrogen, which had risen to 45 mgm% following cardiopulmonary bypass, returned to normal levels prior to discharge from the hospital. He has remained physically active and without symptoms for the past three and one-half years.

Discussion

It is important for the surgeon to understand the developmental anatomy and to be aware of considerable variation in the vascular pattern associated with horseshoe kidney in order to avoid damage to this anomalous structure during the course of surgery.

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During embryologic development, three distinct excretory organs are formed in the human, the pronephros, the mesonephros, and the metanephros. Anatomically, the pronephros is most cranial, the mesonephros intermediate, the metanephros most caudal. All are derived at least in part from the nephrogenic cord which is a mass of retroperitoneal mesoderm situated dorsolaterally in the embryo.[1,2,25]

The pronephros probably never functions in the human,[25] and degenerates completely by the thirtieth day of development.[2] The mesonephros attains considerably better development and probably eliminates some nitrogenous waste. It appears during the middle of the fourth week of development. The mesonephric tubules drain into the mesonephric (Wolffian) duct which drains to the cloaca and is related to the subsequent development of the metanephros.[25]

The metanephros has a dual origin. The collecting system, renal pelvis, and ureter arise from the metanephric diverticulum which buds from the mesonephric duct very near its point of entry into the cloaca. The remainder of the metanephros develops from the caudal aspect of the nephrogenic cord, referred to as the metanephrogenic blastema. Embryologic induction is seen here in that the metanephric diverticulum must induce differentiation of the metanephrogenic mass.[2,22]

During development, the metanephros is situated more caudally than in the adult. The apparent "ascent" is due in part to rapid caudal growth of the embryo which leads to the appearance of actual migration. In addition, the developing kidneys are thought to "slide" forward out of the developing pelvis over the ridges formed by the umbilical arteries below the aortic bifurcation. In so doing, they rotate approximately ninety degrees so that their convex surfaces come to face laterally in the definitive adult position. Horseshoe kidney is thought to develop during the course of ascent when the two renal blastemas are crowded together and fuse, which makes further ascent and rotation impossible. These events occur during the seventh to ninth week of embryonic life.[25]

The blood supply to the primitive nephric tissue is segmental, with disappearance of more cephalad vessels as further caudal development of nephrogenic cord takes place. In the region of the most caudal aspect of the mesonephros, where the definitive kidney will form from the metanephrogenic mass, there is formed an arterial network, termed the rete arteriosum urogenitale, which supplies the suprarenal and urogenital tissues. Eventually a portion of the rete undergoes atrophy with persistence of the adult renal arteries.

The occurrence in adult life of multiple renal arteries, both with and without renal anomalies, is consistent with these embryologic observations.[12] Graves[14] studied the anatomy of the intrarenal vessels by means of angiography and plastic injection. He found that there were five segments in the definitive kidney which were supplied by true end arteries. These findings were confirmed by Sykes.[30] These studies emphasize the segmental nature of accessory renal arteries and the importance of preserving accessory arteries to portions of a horseshoe kidney during the course of surgical management of an associated abdominal aortic aneurysm.

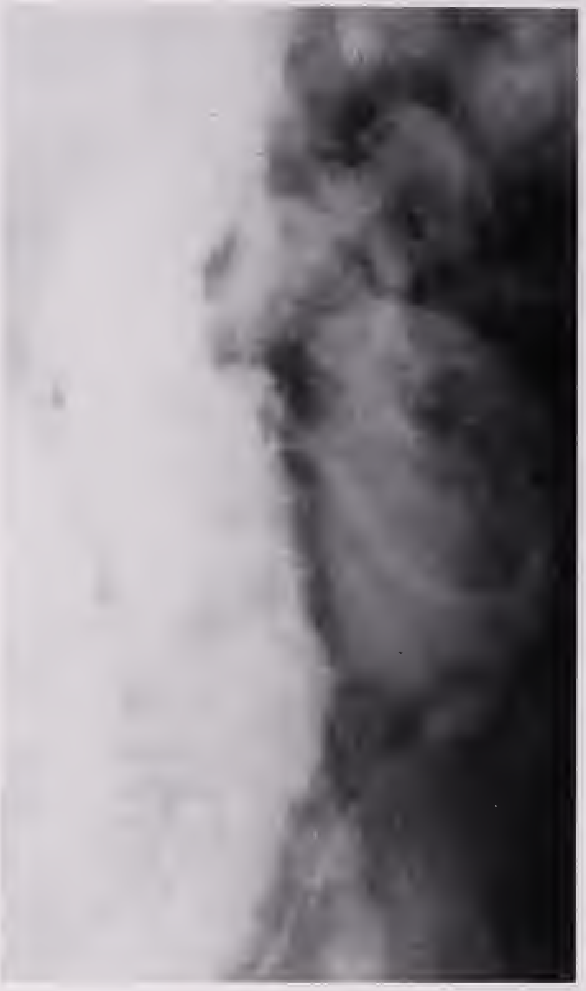

Fig. 1. Abdominal aortogram shows the lumen of the abdominal aortic aneurysm. The two main renal arteries arise from the aorta above the aneurysm and the nephrogram suggests the isthmus of the horseshoe kidney. The aberrant third renal artery is not seen.

Gutierrez[15] in his classical work on the subject of horseshoe kidney, cites the report of Papin based on 223 autopsy cases with this renal anomaly. The number and distribution of renal arteries in this anomaly is extremely variable. The number of arteries supplying the kidney and their frequency in those instances where the exact number was recorded is listed in Table 1. Three to five arteries were demonstrated in two-thirds of the specimens examined emphasizing

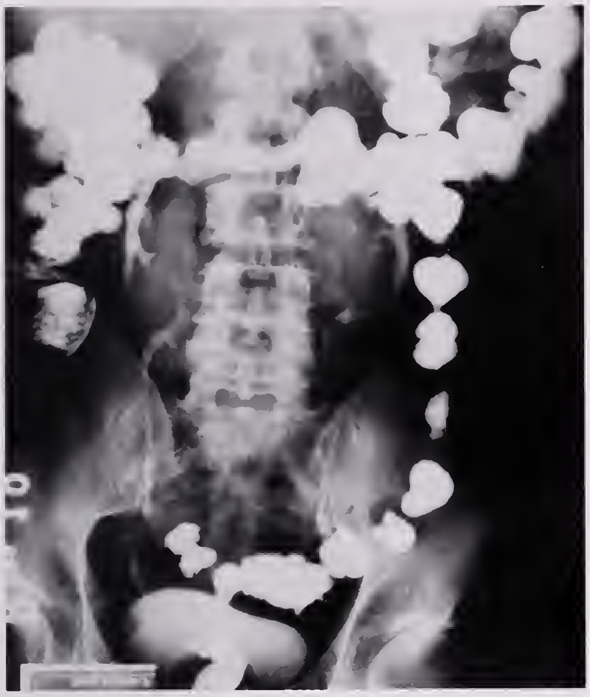

Fig. 2. Intravenous pyelogram demonstrates the characteristic distortion of the renal pelves and ureters associated with the horseshoe kidney.

the complex arterial anatomy which is likely to confront the surgeon.

The number of renal arteries supplying the horseshoe kidney which were identified at the time of surgery for abdominal aortic aneurysm and noted in the collected case reports is also listed in Table 1. The vascular pattern was less complex and the frequency of more than two renal arteries was much less common at surgery than in the autopsy material. This discrepancy can probably be explained, at least in part, on the basis that total discovery of the entire abberant arterial supply of the kidney mass is unnecessary and unwarranted during surgery and only those vessels involved directly with the aneurysm are likely to be identified.

Summary of Previous Experience

The reported experience with aortic aneurysm associated with horseshoe kidney have been reviewed[3-5,7-12,16-24,26-33]—forty cases, including the case presented in this report. There were 35 males and one female patient, with a range in age from 43 to 76, with an average age of 61 years. Three patients presented with rupture, two of whom survived.

In all patients radiographic studies were employed to establish the diagnosis preoperatively. The intravenous pyelogram consistently identified the horseshoe kidney deformity. The presence of characteristic calcification in the aneurysmal wall, when present, provided the physician with the complete diagnosis and supports the concept that an IVP should be routinely employed as part of the workup in all patients with abdominal aortic aneurysm. Retrograde pyelography, though accurate, is rarely required, and only if intravenous pyelography is unsatisfactory.

Aortography can be used to establish the diagnosis of abdominal aortic aneurysm if clinical examination and plain films of the abdomen are in doubt. The associated pyelogram will suggest the horseshoe kidney deformity. Of greater value, however, may be the demonstration of the arterial supply to this anomalous kidney. Aortography was employed in seventeen of the reported cases, however, some mention of the renal arteries was noted in only eleven. The true picture of the renal arterial pattern subsequently found at surgery was displayed in only six[9,12,19,20,22,27] of the preoperative aortograms. Five of these patients had two conventionally situated main renal arteries and only one[19] had an unconventional distribution with three arteries. In our case, the third renal artery arising from the aneurysm and supplying the isthmus was not demonstrated. The value of aortography lies primarily in its ability to determine whether the patient has major right and left renal arteries and whether they arise from the aorta above the aneurysm, from the aneurysm itself or from a major distal vessel. The overlapping vascular structures will generally preclude a thorough angiographic mapping of the renal arteries to a horseshoe kidney even if selective catheterization and multiple views are employed.

In the surgical management of the forty reported cases, resection of the aneurysm with graft replacement was accomplished in thirty-six patients with an operative mortality of six per cent (2 patients). In four instances[5,10,17] no resection was attempted and in one of these[10] the aneurysm was wrapped with mersilene. The renal arteries were neither ligated nor reimplanted in twenty-one instances and the only inconvenience encountered was the need to retract the kidney in order to carry out the operative manuevers.[3,4,9-11,19-27,32,33] In seven instances, one or two minor branches which apparently contributed very little to renal perfusion had to be sacrificed in order to remove the aneurysm.[4,7,10,11,25,26,31] A major renal branch was ligated in two patients[3,23] which necessitated resection of a large segment of the renal mass in each due to infarction. Renal artery reimplantation was carried out for major branches arising from the aneurysm in four cases.[8,16,25,28] In two instances a minor isthmic branch arising from the aneurysm was preserved with a button of aneurysm wall and implanted in the side of the graft used to restore aorto-iliac continuity.[18]

It is apparent that potential complexity of the vascular pattern of the horseshoe kidney rarely precludes successful resection of an abdominal aortic aneurysm. Current technical refinements in renovascular surgery might have permitted salvage of renal parenchyma in the patients subject to major arterial ligation and might have allowed resection in those patients in whom only laparotomy was performed.

The handling of the renal mass itself may be an important aspect of operative therapy of aneurysm and horseshoe kidney. Glen,[13] in reviewing the problems associated with this renal anomaly, noted a high incidence of urinary infection. Damage to the renal pelvis during manipulation or as a consequence of symphysiotomy may spill infected urine in the operative field, with potential disastrous consequences from contamination of the vascular prosthesis. For this reason symphysiotomy should be avoided if at all possible. If this maneuver must be carried out in order to provide adequate exposure for resection, pyelographic delineation of the caliceal systems of the fused kidneys may be helpful to determine the line of division and avoid entrance into the renal drainage system. Fuller has suggested the injection of indigo carmene into one renal artery[11] to define the line of symphysiotomy and avoid devascularization of a portion of the isthmus which may slough and produce a urinary leak.

The renal mass was retracted cephalad or caudad in nineteen cases.[3,4,7-9,12,18,26-28,31] In eleven patients symphysiotomy was carried out[3,10,11,16,20,24,28,29,32,33] and in two others large segments of parenchyma were resected.[3,21] In spite of the potential consequences, no incidence of urinary leak or graft infection was reported in thirteen patients in which the symphyses was divided or a portion of kidney resected. In one instance,[11] an accessory ureter draining the isthmus was ligated and divided without apparent ill effect.

TABLE 1
NUMBER RENAL ARTERIES WITH HORSESHOE KIDNEY

No. of Arteries Per Kidney	No. of Cases with Aneurysm & Horseshoe Kidney at Surgery	No. of Cases of Horseshoe Kidney at Autopsy (Papin/Gutierrez)
1	2	1
2	19	26
3	10	40
4	5	25
5	0	20
6	0	9
7	0	3
8	0	2
10	0	2
Multiple	2	10
13	1	
Not stated	1	
	40	

The low overall operative mortality rate of six per cent[3,7] is remarkable considering the fact that many of these cases posed significant technical difficulties. Two of the three ruptured aneurysms survived.[3,22]

Summary

Abdominal aortic aneurysm associated with horseshoe kidney has been amenable to resection of the aneurysm with preservation of renal integrity in ninety per cent of the cases reported to date. Thirty-four of the thirty-six patients with resection (94%) survived surgery.

An aggressive surgical approach is recommended in spite of the problems imposed by variations in the renal arterial pattern and the inconvenience imposed by the awkward position of the renal mass. An intravenous pyelogram should be performed on all patients prior to surgery for abdominal aortic aneurysm. If a horseshoe kidney is demonstrated, a preoperative aortogram may be helpful to demonstrate the relationship of the main renal arteries to the aneurysm. Angiography will often fail to display the true picture of the renal circulation when multiple arteries are present.

Operative management requires careful manipulation of the kidney, avoidance of symphysiotomy or partial resection if possible and reimplantation of major or accessory renal arteries when feasible.

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Lymphatics, lymphedema and lymphangiosarcoma

Fred A. Deigert, MD, Billings, Montana

The pathophysiology of lymphatic obstruction (lymphedema) is better understood now that lymphangiography is available. Current lymphedema management is also improved. Chronic postmastectomy lymphedema is a causative factor in lymphangiosarcoma.

Because of their close relationship, lymphatics, lymphedema and lymphangiosarcoma are discussed together. There are four purposes for this communication: (1) review of normal lymphatic development, (2) discussion of pathophysiology of lymphedema (particularly postmastectomy lymphedema), (3) review of advances in therapy which have improved management of lymphedema, and (4) discussion of lymphangiosarcoma, a development in some women with chronic postmastectomy lymphedema.

Lymphatic Anatomy and Physiology

Early in fetal development (in the six to nine week old embryo) small avascular buds appear growing off most of the veins (Fig. 1). Soon these buds are infiltrated with lymphocytes and small blood vessels which nourish them to grow as lymph nodes. The buds also extend arm-like channels which interlock with other buds forming a separate drainage system from all parts of the body. This young lymphatic drainage system grows in proportion to fetal growth and becomes a mature system by the time of viability and birth. When the buds fail to join properly they will continue to collect fluid without draining normally into venous junctions (left subclavian-jugular vein site most commonly). The collection grows as the benign tumor, cystic hygroma, of childhood.

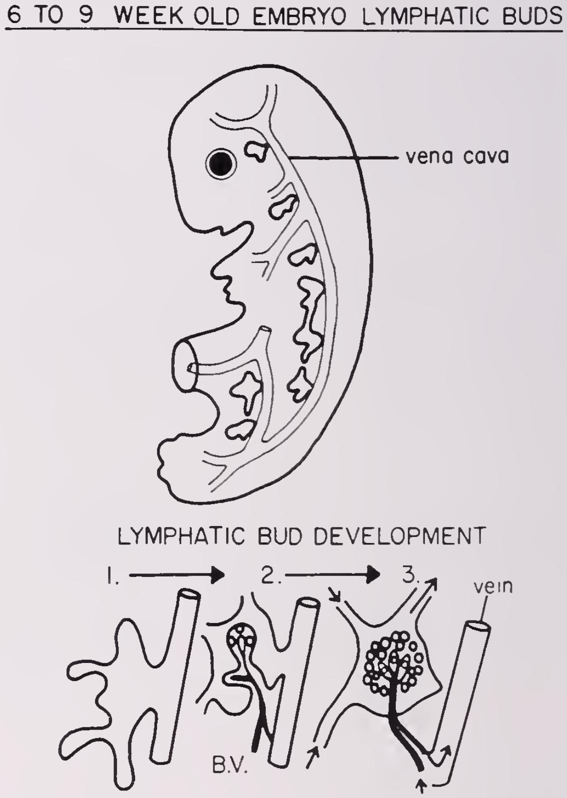
6 TO 9 WEEK OLD EMBRYO LYMPHATIC BUDS
vena cava
LYMPHATIC BUD DEVELOPMENT
1.
2.
3.
vein
B.V.

Fig. 1. Lymphatic system development in the embryo.

As lymphatics branch into tissue, four levels related to size and location are recognized. 1. **Small capillaries** in the skin and in organs are able to collect fluid and larger molecules and cells (protein, dirt, bacteria, cancer, etc.). The osmotic pressure differential helps attract more fluid to fill the vessels. These channels are not visible to the eye. The movement of fluid toward the larger channels is instituted by vessels being squeezed by the interaction of the outer skin tension against the inner muscular contractions. 2. **Medium lymphatic branches** are found subcutaneously and between fascial planes. These contain small one-way valves which permit fluid

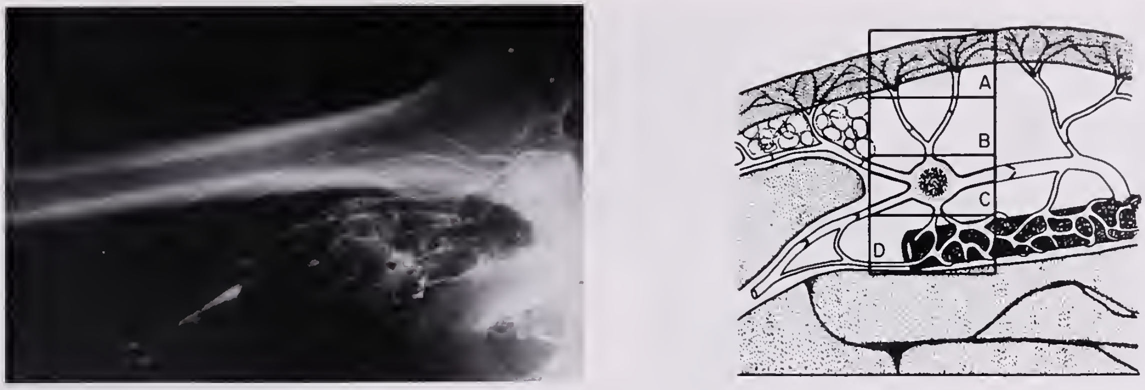

Fig. 2. Mature Lymphatic System
(1) Lymphangiogram, (2) Diagram of System, A. Small Capillaries, B. Medium Lymphatic Vessels, C. Lymph Nodes and Large Vessels, D. Perivascular and Perineural Lymphatics.

and protein content to move toward the heart. The protein concentration in normal vessels is .69 grams/100 ml. fluid.[5] These are the size of fine threads and are the channels seen filled with blue dye during lymphography. (Fig. 2A). 3. **Larger lymphatic channels** the size of strings drain the **lymph nodes** from the hilum (See Fig. 2B). These have very competent valves and continue to get larger as they progress toward the thoracic duct which drains lymph from the lower body through the chest to the subclavian vein junction in the neck. 4. **Perivascular and perineural communications** represent a network of small caliber collateral lymphatics which lie within the perivascular neural sheaths. These channel only small amounts of fluid normally but can increase and convey larger amounts under certain conditions (lymphedema).

Lymphography has increased our knowledge of structure and function of this system. Colloidal particles in blue dye are injected into the web between the toes. They are picked up by small lymphatic capillaries and carried to the medium size channels. The dorsum of the foot is exposed with an excision which extends into the subcutaneous level. Here the blue, thread-sized, dye filled vessels are seen and catheterized with small bore needles. (The procedure has been likened to performing a barium enema on an ant.) The oily ethiodol contrast is slowly injected (usually 15-30 cc. into each foot) over a half hour period of time. This fills larger lymphatic channels and also lymph nodes in the pelvis and retroperitoneum over the next six to twelve hours. These medium vessels enter the lymph nodes at the periphery and flow 1° around the edge and also through the center.

Pathophysiology of Lymphedema

Obstruction or interruption of lymphatics causes stasis of fluid. Collateral channels will try to reroute this fluid (dermal backflow) if they are available. Subsequent enlargement of medium size channels causes poor valvular contact and more stasis occurs. Gravity then plays an important role in the movement of fluid. The fluid becomes more viscous (jelly-like) as the protein concentration increases to four times normal. If sufficient collateral circulation is present lymphedema will be transient. If not, then chronic inflammatory changes in the vessels and tissue are seen and permanent lymphedema occurs.

Most articles arbitrarily divide lymphedema into two categories as determined by etiology: primary (congenital) and secondary (infections, inflammation, disease, and trauma). However, most of the time we are confronted with post-surgical lymphadenectomy lymphedema, and most specifically that which is seen in the arm

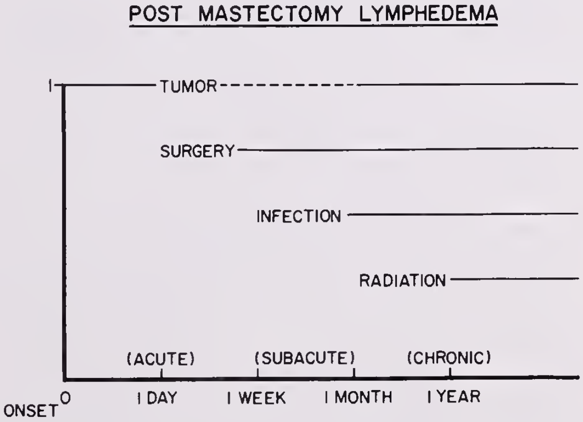

Fig. 3. The time of onset of lymphedema helps determine which factors caused it.

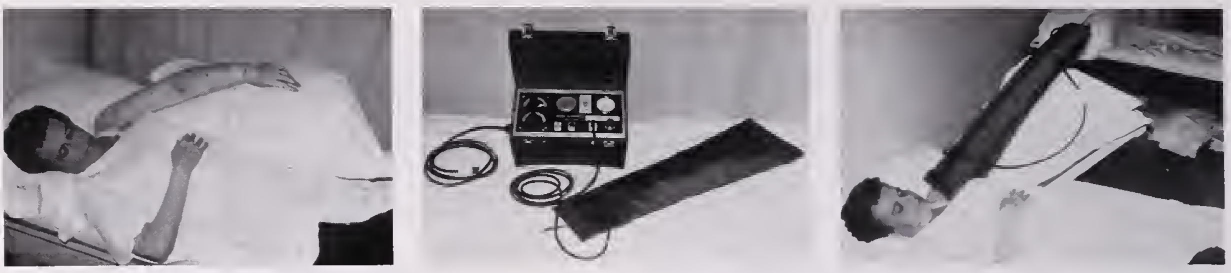

Fig. 4. A. Lymphedematous arm *B. Jobst pressure sleeve* *C. Applied to patient*

after breast cancer surgery—post mastectomy lymphedema.

Many have argued as to the relative causative role played by surgery, radiation, infection, and tumor. In fact, each can cause lymphedema alone, but in most situations, two or more factors play a compromising role.[7] The time of onset of lymphedema or sudden increase tells us which factors predominate. (Fig. 3) If it occurs prior to treatment the cause is tumor invading lymph nodes. At one day post-op the cause is surgical removal of lymphatics during dissection. By leaving the axillary vein sheath intact, collateral lymphatics will be spared and incidence of lymphedema significantly lowered.[4] If onset is at one week postoperative, look for infection and delay of flap healing and fluid accumulation as the causes. Axillary vein thrombophlebitis may be involved but usually it is not. If post-op irradiation was given, at one month,sufficient irritation of lymphatics may be seen to contribute to the obstructive process. At one year persistent edema from any or all of these factors becomes chronic, firm and brawny. Any sudden increase may be due to infection—lymphangitis or recurrent cancer.

Management of Lymphedema

Most successful treatment programs include prophylactic instruction to the patient on fingernail care, avoidance of sunburn and injury, reminding technicians not to draw blood or take blood pressures in the affected arm, and exercise to keep the muscular tone. Added measures such as properly fitted elastic arm sleeves and occasional diuretic and antibiotic therapy as needed are also appropriate.

Recent physical therapy advances assist removal of static fluid in extremities. Jobst pressure sleeves with intermittent pressure applied to the arm (60-80 mm. Hg) for 45 seconds, then rest 15 seconds, for several hours daily will significantly reduce swelling (Fig. 4). The edema can be kept at a low level by using a pressure gradient elastic sleeve tailored to the patient's measurements or elastic arm wrap after squeezing out the jelly-like fluid with the Jobst treatment.[5] The surgical approach of implanting sterile strings or grafts has been tried with some success but in most cases this is not necessary if an active physical therapy program is followed.[3]

Lymphangiosarcoma

Rarely a very malignant lymphatic tumor will appear on the edematous extremity. This is only seen in 1:500 patients with breast cancer and in only 1:300 women in actuality because only this per cent will survive five to ten years which is the usual time delay before appearance. Furthermore, only one-third of these will have significant lymphedema, a necessary predisposing factor.[1]

The clinical appearance is usually a solid, firm nodule on the upper inner arm. It is often discolored blue from vascular invasion and hemorrhage. Since it is often multifocal, other lesions can be seen on the arm (Fig. 5A). The differential diagnosis includes (1) dermal metastasis from breast carcinoma (biopsy needed), (2) herpes zoster (more vesicular and distributed along the neurodermatome), (3) psoriasis (more scaley and silver crusts), (4) chronic granulocytic leukemia (not confined to the arm), (5) reticulum cell sarcoma (biopsy needed), (6) mycosis fungoides (other parts of body, biopsy), (7) kaposi sarcoma (bilateral, biopsy), and (8) malignant hemangioma (biopsy).

At histologic examination, along with the signs of chronic lymphedema (proliferating lymphatics, lymphocyte infiltration and fluid spaces), there are plump malignant endothelial cells with frequent mitosis lining the lymphatic spaces. Vascular invasion causes red blood cells to accumulate giving the "bruised look" color to the clinical appearance.

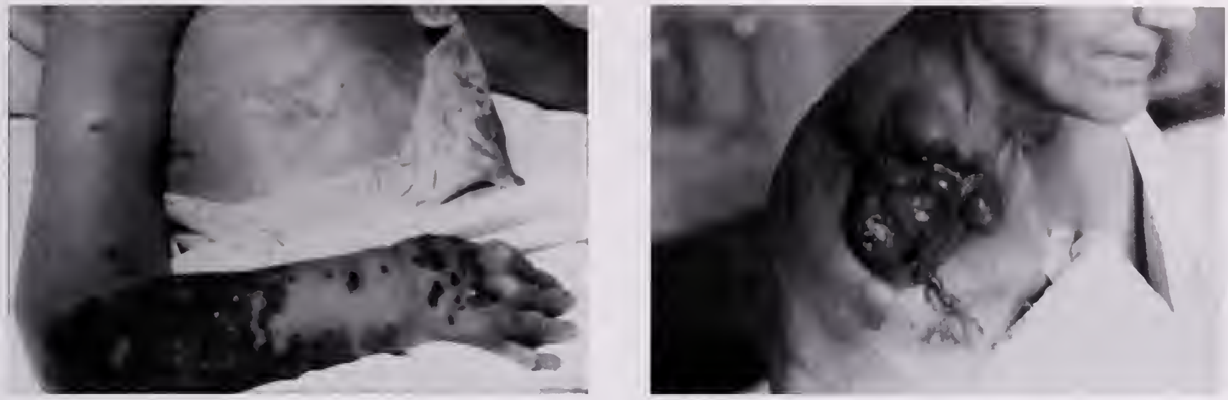

Fig. 5. A. Multifocal lymphangiosarcoma

B. Shoulder recurrence after amputation

The rationale for treatment of lymphangiosarcoma must be based on the usual clinical course. This multifocal tumor will occur on any or many parts of the arm and spread up to the shoulder. Lung metastasis usually occurs within one year of diagnosis, and the average survival is 19 months. (Ranges from 2-66 months.) Approximately 100 cases are reported in the literature, and the five year survival rate is five to ten per cent.[1]

Surgical amputation is usually recommended because of the multifocal nature of the tumor. However, stump recurrences occur and many women refuse this type of treatment particularly when the effort is only palliative (Fig. 5-B). Wide local excision will have difficulty healing in an edematous extremity, but excisional biopsy can usually be done. Radiation to moderate doses of 3000 to 5000 Rads has been shown to retard tumor growth, but booster doses to localized areas of 6000 to 7000 Rads in six to eight weeks are needed to be tumorcidal. This amount of radiation causes radiodermatitis as a temporary side effect. Again, this type therapy is usually palliative, but several long term survivors are reported.[2] Drug therapy with cytotoxic agents is limited to growth restraint only. Cytoxan should be tried first because of two short temporary responses reported. Combination programs with newer agents should be tried because no outstanding success has been obtained to date. This program would probably include Cytoxan.[6]

We believe the best results are obtained when treatment is based upon the clinical situation. When there are one or few localized arm nodules, try excision and postoperative irradiation to a wider area to 5000 to 7000 Rads in five to seven weeks, depending on reaction, with curative intent. When there are many arm nodules, amputation is the most appropriate treatment, and reserve whole arm irradiation for those who refuse. When there is chest wall, lung or bone metastasis, try Cytoxan alone or in combination with newer drugs.

Summary

Lymphatic anatomy and pathophysiology are better understood since development of lymphangiography. Postmastectomy lymphedema occurs when lymphatic channels are interrupted and when collateral circulation is impaired. Chronic lymphedema predisposes to a rare cancer—lymphangiosarcoma. Treatment of this tumor is usually palliative and is directed toward minimizing the supportive care required during the short survival time of these patients.

ACKNOWLEDGEMENT

Photos courtesy Dr. Robert Coltz, University of Minnesota.

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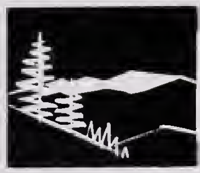

COLORADO

Sando Elected

Isamu Sando, MD, associate professor and director of the research division, University of Colorado Department of Otolaryngology, has been elected to the Barany Society, an international organization which has its headquarters in Uppsala, Sweden. Doctor Sando is noted for his work on the pathology of the vestibular system in human temporal bones. Doctor Sando completed medical school and otolaryngology residency at the Nihon University School of Medicine, Tokyo, Japan. He is a member of the American Otological Society and the Japan Society for Equilibrium Research. The Barany Society is named after Dr. Robert Barany, professor at the University of Uppsala, Sweden, and 1914 Nobel prize winner in medicine.

Doctor Lemon Cited

John C. Lemon, MD, Englewood, Colorado, a member of the Colorado and Denver Medical Societies, has been cited by the American College of Radiology as a fellow for his distinguished achievements. Doctor Lemon is affiliated with Mercy Hospital, Denver, and is a 1955 graduate of Washington University School of Medicine at St. Louis, Mo. The fellowship was awarded at the ACR annual meeting and Convocation in Portland, Oregon, late in March.

MEDICAL SCHOOL NOTES

University of Nevada School of Medical Sciences

Electron Microscope Acquired

Gifts totaling $46,000 have enabled purchase of an electron microscope for use in teaching, diagnosis, and research. An Hitachi H.U. 125E model, capable of magnifying a cell membrane to a quarter inch, has been installed in Mackay Science Hall through the generosity of the Luke B. Hancock Foundation, the Wilbur May Foundation, the Timken-Sturgis Foundation, H. Edward Manville, and the Ed and Mary Van Tobel Foundation.

* * *

First Graduate

Captain Michael G. Kinnison, now a member of the U.S. Air Force at Keesler Air Force Base, Biloxi, Mississippi, was awarded the first doctor of medicine degree from the new University of Nevada School of Medical Sciences on December 13, 1974. Through an accelerated course Captain Kinnison was able to complete his work a semester ahead of his normal classmates. Kinnison had received honors in both medicine and neurology at the University of Colorado in previous studies.

A Team Approach to the Treatment of the Arthritic Patient

A three day seminar will be held June 26, 27, and 28 at the Rose Hospital Auditorium, located in the Joe and Betty Alpert Arthritis Treatment Center. On June 27 and 28, Dr. John Calabro, professor of medicine at the University of Massachusetts and director of the Arthritis Division of Worchester County Hospital, will speak on "Arthritis and Children." Professor Harold S. Robinson from the University of British Columbia, Canada, will speak June 27 and 28 on "A Team Approach to Arthritis in a Canadian Province." On June 28, Professor Clement Sledge, professor of surgery at the Harvard School of Medicine in Boston will talk on "Total Knee Replacement."

The seminar is being co-sponsored by Rose Hospital, the University of Colorado Medical Center, the Regional Arthritis Program of RMP and the Rocky Mountain Chapter of The Arthritis Foundation. Registration will be limited. To register, please contact the Office of Post Graduate Medical Education at the University of Colorado, 394-8406 or 394-7376.

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TUESDAY, MAY 13

10:00 a.m. New Mexico Foundation for Medical Care — PSRO — Board Meetings

2:30 p.m. Council Meeting

WEDNESDAY, MAY 14

9:00 a.m. Program for New Members

2:00 p.m. First Meeting of House of Delegates

6:30 p.m. Convention Reception
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THURSDAY, MAY 15 BASIC CONCEPTS IN ONCOLOGY

8:30 a.m. - 12:00 Viral and Other Factors in Oncogenesis
Paul Black, MD, Associate Professor of Medicine, Harvard University School of Medicine; Associate Physician, Massachusetts General Hospital, Boston, Massachusetts

Kinetics of Normal and Malignant Cells
Emil Frei III, MD, Physician-in-Chief, Children's Cancer Research Foundation, Professor of Medicine, Harvard University School of Medicine, Boston, Massachusetts

Immunity and Cancer
Lynn E. Spitler, MD, Assistant Professor of Medicine in Residence, and Research Associate, Cancer Research Institute, University of California School of Medicine, San Francisco, California

THURSDAY
(cont.)

DIAGNOSTIC METHODS IN ONCOLOGY

2:00 p.m. - 5:00 p.m.

Cancer Surveillance — the Present Status
Charles R. Key, MD, Associate Professor of Pathology, University of New Mexico School of Medicine; Medical Director, New Mexico Tumor Registry; Assistant Director, University of New Mexico Cancer Research and Treatment Center, Albuquerque

Blood Tests for Cancer
Robert Strickland, MD, Chief, Division of Gastroenterology, and Assistant Professor of Medicine, University of New Mexico School of Medicine, Albuquerque

Cytological Techniques
Robert List, MD, Department of Pathology, St. Joseph Hospital, Albuquerque

Advances in Cancer Diagnostics: Radiograph, Ultrasonography, and Scintigraphy
Jon Shoop, MD, Associate Professor of Radiology, University of New Mexico School of Medicine, Associate Professor of Pharmacy, Albuquerque

6:30 p.m. **Reception and Presidential Banquet**

FRIDAY, MAY 16

PRINCIPLES OF CANCER MANAGEMENT

9:00 a.m. - 12:00 noon

Modern Concepts in Cancer Surgery
John S. Stehlin, MD, Clinical Associate, Professor of Surgery, Baylor College of Medicine; Scientific Director, St. Joseph Laboratories for Cancer Research, Houston, Texas

The Role of Chemotherapy
Emil Frei III, MD

Radiotherapy
Morton Kligerman, MD, Professor and Chief, Division of Radiotherapy, University of New Mexico School of Medicine; Director, Cancer Research and Treatment Center, University of New Mexico School of Medicine, Albuquerque

2:00 p.m. **Second Meeting of House of Delegates**

6:00 p.m. **Specialty Society Meetings**

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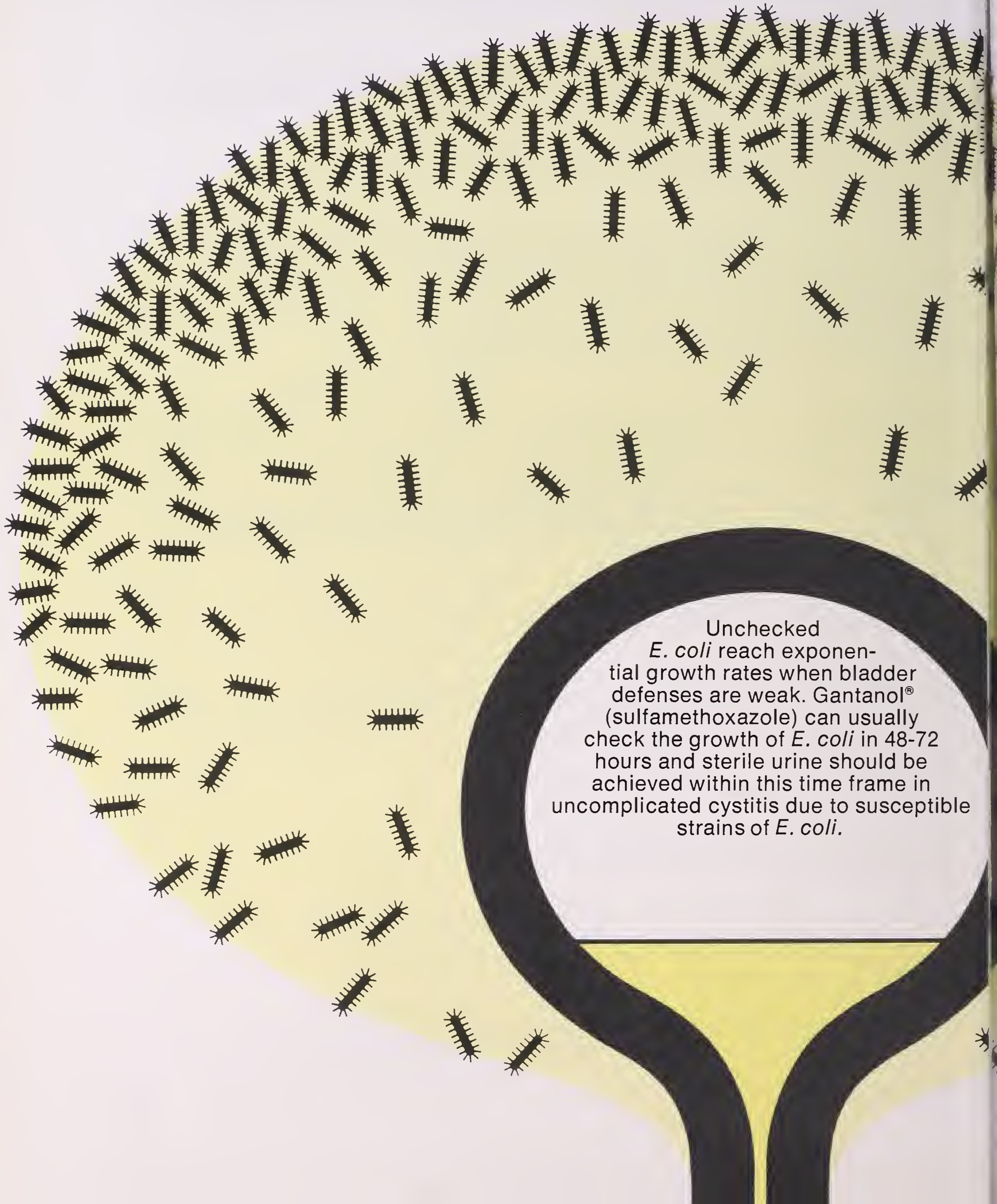

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Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

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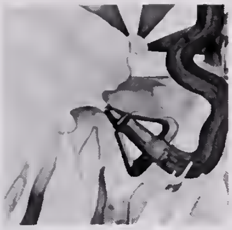

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Medical Department, Box 5110, Chicago, Ill. 60680 481

THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Accreditation Manual for Long Term Care Facilities: Joint Commission on Accreditation of Hospitals. 2nd ed. JCAH, 1975. 30 p. Gift.

Acupuncture Anaesthesia: National Institutes of Health, Geographic Health Studies Program. U.S. Govt. Printing Office, 1975. 339 p. Gift.

Anatomy of the Human Body: Henry Gray. 29th American ed. Lea & Febiger, 1973. 1466 p. $28.50.

The Anatomy of the Ocular Adnexa: Frederick A. Mausolf. Thomas, 1975. 49 p. $4.95.

Atopic Dermatitis: Georg Rajka. Saunders, 1975. 165 p. (Major problems in dermatology, v. 3)

Cataract Surgery: Norman S. Jaffe. Mosby, 1972. 417 p. $47.50.

Chromosomes and Cancer: James German, ed. Wiley, 1974. 756 p. $31.50. Gift of the American Cancer Society.

Electroencephalography (EEG) of Human Sleep, Clinical Applications: Robert L. Williams. Wiley, 1974. 169 p. $15.00.

Exercise and Coronary Heart Disease: Gerald F. Fletcher. Thomas, 1974. 245 p. $15.00.

Geriatric Medicine: W. F. Anderson and T. G. Judge, eds. Academic Press, 1974. 328 p. $12.50.

Hemispheric Disconnection and Cerebral Function: 3rd Cerebral Function Symposium, Coronado, Calif. Thomas, 1974.

Intractable Pain: Mark Mehta. Saunders, 1973. 287 p. (Major problems in anesthesia, v. 2)

Medical Disorders in Obstetric Practice: Cyril G. Barnes. Blackwell, 1974. 509 p. $24.50.

Mucosal Biopsy of the Gastrointestinal Tract: Richard Whitehead. Saunders, 1973. 202 p. (Major problems in pathology, v. 3)

Multiple Sclerosis, A Reappraisal: Douglas McAlpine, Charles E. Lumsden and E. D. Acheson. 2nd ed. Williams and Wilkins, 1972. 653 p. $21.50.

Muscle Relaxants: Stanley Feldman. Saunders, 1973. 190 p. (Major problems in anesthesia, v. 1)

Neurological Surgery, A Comprehensive Reference Guide to the Diagnosis and Management of Neurosurgical Problems: Julian R. Youmans, ed. Saunders, 1973. 3 v. $114.00.

The Physician's Assistant: Ann S. Ford. Praeger, 1975. 245 p. $17.50.

The Physician's Assistant, Today and Tomorrow: Alfred M. Sadler. Yale University Press, 1972. 256 p. $2.37.

Plastic and Reconstructive Surgery of the Face and Neck: John Conley and John T. Dickinson, eds. Grune & Stratton, 1972. (1st International Symposium on Plastic and Reconstructive Surgery in the Face and Neck, New York, 1970) 368 p. (V. 2, Rehabilitative surgery) $19.80.

Poisoning By Drugs and Chemicals, Plants and Animals; An Index of Toxic Effects and Their Treatment: Peter Cooper. 3rd ed., rev. and enl. Year Book Medical Publishers, 1974. 218 p. $12.56.

Symposium on Glaucoma. Mosby, 1975. 382 p. $36.00.

Techniques of Family Psychotherapy: Donald A. Bloch, ed. Grune & Stratton, 1973, 124 p. $4.50.

The library wishes to express appreciation for the contribution received from the Rocky Mountain Chapter of the Western Orthopedic Association.

Book Review

Clinical Perinatology: Silvio Aladjem, MD, FACOG, and Audrey K. Brown, MD, Editors, C. V. Mosby, 1974. 488 p., $39.50.

At $14.20 a pound, *Clinical Perinatology,* edited by Silvio Aladjem and Audrey K. Brown is a bargain.

From the foreword to the conclusions this 442-page C. V. Mosby publication shakes off the categorical cobwebs that shroud many textbooks of similar vintage. In a logical human biology style the editors have successfully woven contrasting strands of perinatal philosophy, physiology and practical staff into one strong bolt of information.

The late Dr. Virginia Apgar leads off with a perspective on the continuum of perinatology. The first two chapters blend the physiology and pathophysiology of pregnancy from the maternal viewpoint. Dr. Aladjem presents the fetus as a patient, a theme that Dr. Apgar always preached, with refreshing summaries of some of the newer techniques in assessing fetal status. An extensive chapter on perinatal genetic studies and counseling includes a valuable appendix of resource people from throughout the U.S.A.

At a time when the eye of the malpractice storm is moving inexorably toward perinatal shores, Irving Ladimer's chapter on legal and ethical considerations is right on.

Chapters on perinatal infection and perinatal pathology are overlapping in small part but basic enough to be reinforcing. The placenta is presented by the morphologist and the physiologist in such a way to erase the myth of the inert placental barrier.

Labor stress and optimal management systems are dealt with in logical sequences that offer resources for planning and development of new or renovated perinatal units.

June Brady and George Cassady provide eloquent closing chapters on the homeostatic adjustment of the fetus and neonate and the impact of neonatal intensive care on the quality of life.

Sandwiched between chapters 13 and 15 is a practical view of the predictive indices of neonatal morbidity and mortality that are essential for comparing outcome among diverse populations.

After these generally glowing reactions to the book it is unfortunate to end on a complaining note.

Having served on the AMA Committee on Maternal and Child Care that generated the epochal policy statement of the House of Delegates on centralized and/or regionalized perinatal care, I fully expected to find at least mention of that position in the final chapter. Instead there was comment on the Nurses' Association of the American College of "Obstetrics and Gynecology", the American Academy of Pediatrics, Inhalation Therapists, Nurse Anesthetists, and EMT's!

For all the leadership and man-hours invested by the AMA, the ACOG, and the AAFP, the blatant omission of the input of these professionals is a serious oversight and a reinforcement of the old adage that an ivory tower is still a womb with a view — one view.

L. Joseph Butterfield, MD

OBITUARIES

James A. Stapleton, MD, died Monday, March 17, 1975, at the Denver Presbyterian Medical Center after a brief illness. He was a native Denverite, born here, June 22, 1913. He received his MD from the University of Colorado School of Medicine in 1938, interned at Denver General Hospital, and served a residency in general surgery at Colorado General Hospital.

He received an MS in surgery from the University of Colorado in 1940. After serving in the Army Medical Corps during World War II, he became a Fellow in surgery at the University of Colorado Medical Center in 1945, then chief surgical resident in 1946. He was on the active staffs of Rose Memorial and Mercy hospitals and associate staff of St. Luke's. He was on the associate attending staff at Colorado General Hospital and held the academic rank of Assistant Clinical Professor of Surgery at the University of Colorado Medical Center.

He was formerly a member of the Denver and Colorado Medical societies and of the American Medical Association. He belonged to the Denver Academy of Surgery, serving as its president for a year. He was certified by the American Board of Surgery, and was a fellow of the American College of Surgeons. He was also a member of the Southwestern Surgical Congress.

Doctor Stapleton was married to Leonore Haeger of Denver, and Mrs. Stapleton survives him as do a daughter, Mrs. Leonore S. Mossman, Valencia, California; a sister, Mrs. Betty Mattson; and a brother, C. Ben Stapleton, both of Denver. Two grandchildren of Valencia, California, also survive.

Duncan D. Monroe, MD, died in Sterling, Colorado, at the age of 101 years. He was born in Durham, Iowa, October 12, 1873; his family moved to Illinois in 1880. He attended Rush Medical College in Chicago, receiving his MD in 1901.

He practiced general medicine in Hillrose, Illinois, until 1910 when he moved to the state of Washington. He joined the armed forces during World War I, and served a year with the expeditionary forces in France. Following the war he joined the staff of the Veterans Administration Hospital in Seattle, Washington. Later he became superintendent of the Madison County Tubercular Sanitorium, Edwardsville, Illinois.

In 1936 he opened an office in Alton, Illinois, and practiced general medicine until his retirement in 1952.

In 1957 he moved to Sterling, Colorado.

He belonged to the American Medical Association and the Illinois State Medical Society, and was an honorary member of the Colorado Medical Society. He was a very active Mason and belonged to the Logan County Historical Society and the Sterling American Legion Post. He was a Methodist.

Doctor Monroe was married to Arvilla Stockton in Sterling in 1900. She died in 1938. He was married to Alberta Martin in Alton, Illinois in 1957, and she survives him. Also surviving are four sons, Clarence, Waverly, Ohio; Wray, Tyron, North Carolina; Rex, Arcadia, California; and Robert, Kensington, Maryland; and three daughters, Mrs. Frances Manyk, Denver; Mrs. Mary Swinnery, Alton, Illinois; and Mrs. Shirley Campion, Granite City, Illinois. The doctor left sixteen grandchildren and fourteen great grandchildren.

* * *

Montana

F. Hughes Crago, MD, Great Falls, Montana, died February 22, 1975, at the age of 66. In 1939 Doctor Crago became associated with the Great Falls Clinic. Since 1940 he was a member of the Montana Medical Association and the Cascade County Medical Society. He was also a member of the American Medical Association. He had been elected to a fellowship in the American College of Physicians. He was a fellow of the American Diabetes Association and the American Heart Association. He is survived by Mrs. Mary Crago, four daughters, six grandchildren, and two brothers and two sisters.

* * *

Wilfrid A. McCannel, MD, of Chinook, died February 1, 1975, at the age of 75. He was born in Toronto, Canada, and was graduated from the University of Toronto. He had been a member of the Montana Medical Association and the Hill County Medical Society since 1932. He is survived by his wife, four sons, two grandchildren, and two sisters.

MEETINGS

St. Joseph Hospital

6TH ANNUAL INDUSTRIAL HEALTH CONFERENCE

1835 Franklin Street, Denver, Colorado

May 15, 1975

Contact: Hospital Community Relations Department, 1835 Franklin Street, Denver, Colorado 80218

American College of Surgeons

ANNUAL MEETING, NEW MEXICO-EL PASO CHAPTER

Hilton Inn, Albuquerque, New Mexico

May 17-18, 1975

Contact: William J. Langlois, MD, 717 Encino Place, NE, No. 5, Albuquerque, New Mexico 87102.

American College of Sports Medicine

TWENTY-SECOND ANNUAL MEETING

Marriott Hotel, New Orleans, Louisiana

May 22-24, 1975

Contact: Gary R. Jenks, 1440 Monroe St., Madison, Wisconsin 53706

National Asthma Center

1975 SYMPOSIUM ON ASTHMA AND ALLERGY

Cosmopolitan Hotel, Denver, Colorado

May 28-30, 1975

Contact: Elliott Middleton, Jr., MD, 1999 Julian St., Denver, Colorado 80204

American College of Cardiology

ISCHEMIC HEART DISEASE: A CRITICAL OVERVIEW

Golden Gateway Holiday Inn,
San Francisco, California

May 29-31, 1975

Contact: American College of Cardiology, c/o Mary Anne McInerny, 9650 Rockville Pike, Bethesda, Maryland 20014

Estes Park Institute

CREATIVE LEADERSHIP IN HEALTH CARE FACILITIES

YMCA Conference Center, Estes Park, Colorado

June 1-4, 1975

Contact: C. Wesley Eisele, MD, P.O. Box 400, Englewood, Colorado 80110

Rocky Mountain Neurosurgical Society

TENTH ANNUAL MEETING

Hotel Cozumel Cariebe, Cozumel Island, Yucutan Peninsula, Mexico

June 8-11, 1975

Contact: Richard H. Moiel, MD, 601 Medical Towers, 1709 Dryden St., Houston, Texas 77025.

American Geriatrics Society

A DAY IN GERIATRIC THERAPEUTICS

Stouffer's Denver Inn, 3203 Quebec,
Denver, Colorado

June 17, 1975

Contact: Frank McGlone, MD, 701 East Colfax Ave., Denver, Colorado 80203

Credit: 6 hours AAFP

University of Colorado Medical Center

PATHOLOGY IN GYNECOLOGY AND OBSTETRICS

Given Institute of Pathobiology
Aspen, Colorado

June 30 - July 4, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

Colorado Academy of Family Physicians

ANNUAL MEETING

Manor Vail, Vail, Colorado

July 11-13, 1975

Contact: Mrs. Shirlee Myers, 1601 East 19th Avenue, Denver, Colorado 80218

American Academy of Family Physicians

18TH ANNUAL RUIDOSO SUMMER CLINIC

Ruidoso, New Mexico

July 14-17, 1975

Contact: Bob Reid, P.O. Box 456, Sunland Park, New Mexico 88063

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CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines
WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**
Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy
Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development.)

All tetracyclines form a stable calcium complex in any bone-forming tissue. A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued

Tetracyclines are present in milk of lactating women taking tetracyclines.

To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug. The anti-anabolic action of tetracyclines may increase BUN While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.

Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.
PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic)

Treat all Group A beta-hemolytic streptococcal infections for at least 10 days

Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin
ADVERSE REACTIONS: **Gastrointestinal** (oral and parenteral forms) anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region.
Skin: maculopapular and erythematous rashes, exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**)
Renal toxicity: rise in BUN apparently dose related (See **WARNINGS**)
Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus.

Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued
Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia

Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands, no abnormalities of thyroid function studies are known to occur
USUAL DOSAGE: **Adults** — 600 mg daily, divided into two or four equally spaced doses. More severe infections an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea In uncomplicated gonorrhea, when penicillin is contraindicated, 'Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule 900 mg initially, followed by 300 mg q i d for a total of 5 4 grams.

For treatment of syphilis, when penicillin is contraindicated, a total of 18 to 24 grams of 'Rondomycin' (methacycline HCl) in equally divided doses over a period of 10-15 days should be given. Close follow-up, including laboratory tests, is recommended

Eaton Agent pneumonia 900 mg daily for six days
Children — 3 to 6 mg/lb/day divided into two to four equally spaced doses.

Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided
Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated. Food and some dairy products also interfere Give drug one hour before or two hours after meals. Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding

In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses

In streptococcal infections, a therapeutic dose should be given for at least 10 days.
SUPPLIED: Rondomycin' (methacycline HCl) 150 mg and 300 mg capsules, syrup containing 75 mg/5 cc methacycline HCl.

Before prescribing, consult package circular or latest PDR information.

Rev. 6/73

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*This drug has been evaluated as "probably" effective for this indication.

See brief summary of prescribing information on facing page for Indications, Contraindications, Warnings, Precautions and Adverse Reactions.

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a nonsalicylate analgesic equal to aspirin for relief of pain,[1,2] yet unlikely to cause the gastric irritation,[2,3] allergic reactions[2] or increased bleeding time[4] associated with aspirin therapy...

and a skeletal muscle relaxant shown in extensive clinical studies to afford relief of discomfort in acute musculoskeletal conditions*[5-7] but which is not an antihistamine or tranquilizer derivative and is unlikely to produce a tranquilizing or sedative effect.[5,7,8]

***Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.
Warnings: *Usage in Pregnancy*—Use in women of childbearing potential only when potential benefits outweigh possible risks.
Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.
Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-four patients, it was not possible to state that the dysfunction was or was not drug induced.
Usual Adult Dosage: Two tablets q.i.d.
Supplied: Scored, light green tablets, imprinted "McNEIL"—bottles of 100.

References: 1. Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 1955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, F.N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: New Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboratories, Inc.

†U.S. Patent No. 2,895,877

McNEIL McNeil Laboratories, Inc.
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MEDICAL SPACE. East Mississippi Professional Park in Aurora. Predominately medical and dental building. Equity positions also available. Contact: TOM HOLDSWORTH, Grubb and Ellis Company, Denver, Colorado. (303) 572-7700. 475-8-3B

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

WARNING
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Indications: This combination drug finds its usefulness primarily in the treatment of edema. Any usefulness of triamterene when used with a thiazide in hypertension will derive from its potassium-sparing effect. Either its main diuretic effect or potassium-sparing effect when used with a thiazide drug should be determined by individual titration. (See box warning.)

Edema associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. Also, mild to moderate hypertension.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used comcomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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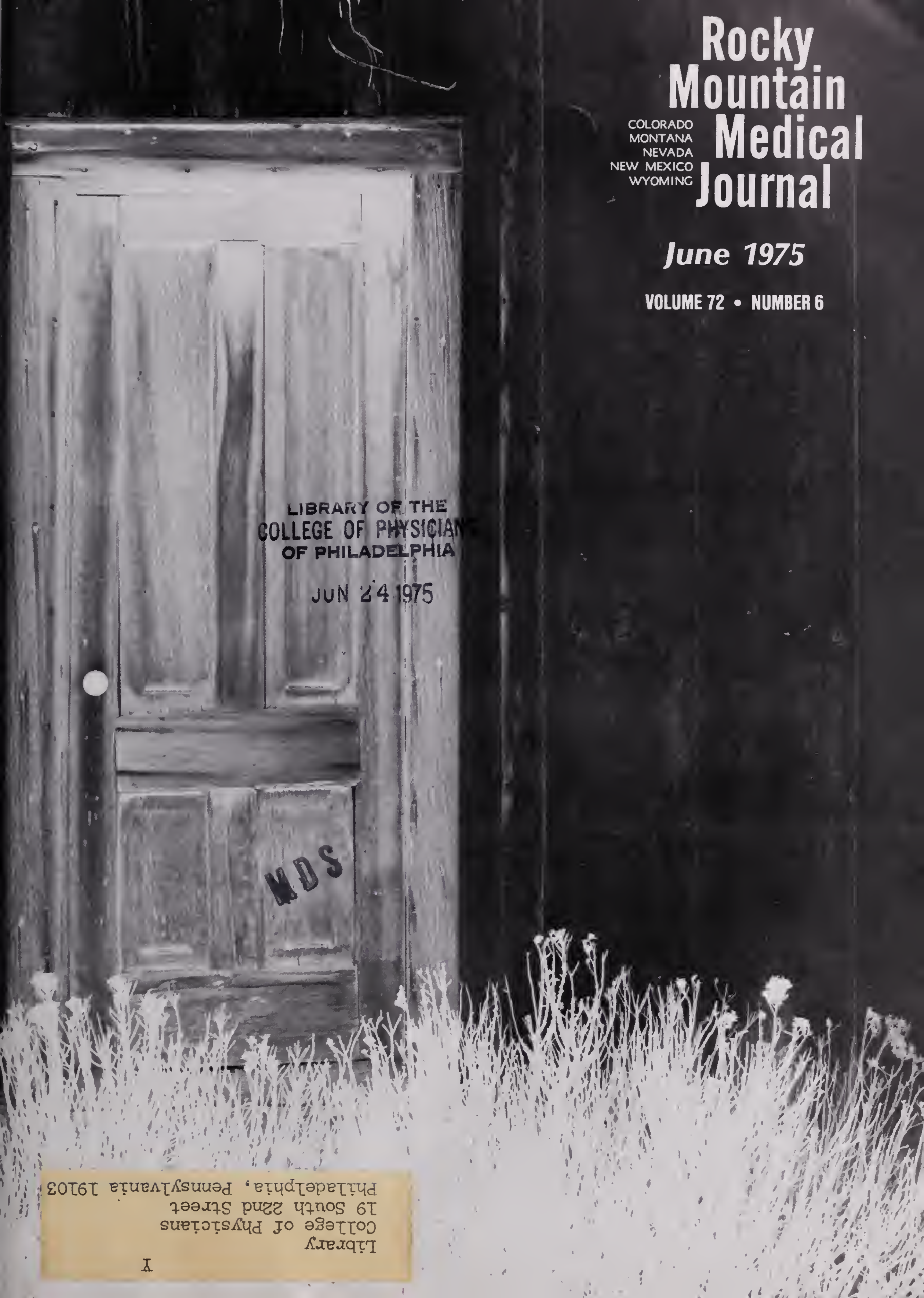

Rocky Mountain Medical Journal

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*Higgs, R. H., Smyth, R. D., and Castell, D. O., Gastric Alkalinization—Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin, *The New Engl. J. of Med.*, 291, 486-490, 1974.

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OUR COVER

June is the door to summer, an opening out on dazzling mornings in the mountains, on vegetable gardens to be tended, on the incomparably reviving tonic of fresh mountain air. The door can swing open to disclose trails and subsequent disclosures of mountains and lakes. The door opens for time in the sun, time to generate meaningful activities as well as for time to be lazy. Doors are full of mystery in the winter when they are unfailingly closed. Summer's doors open on such beautiful mornings that they keep us alive and expectant. Credit: Tony Mendlin, Reno, Nevada.

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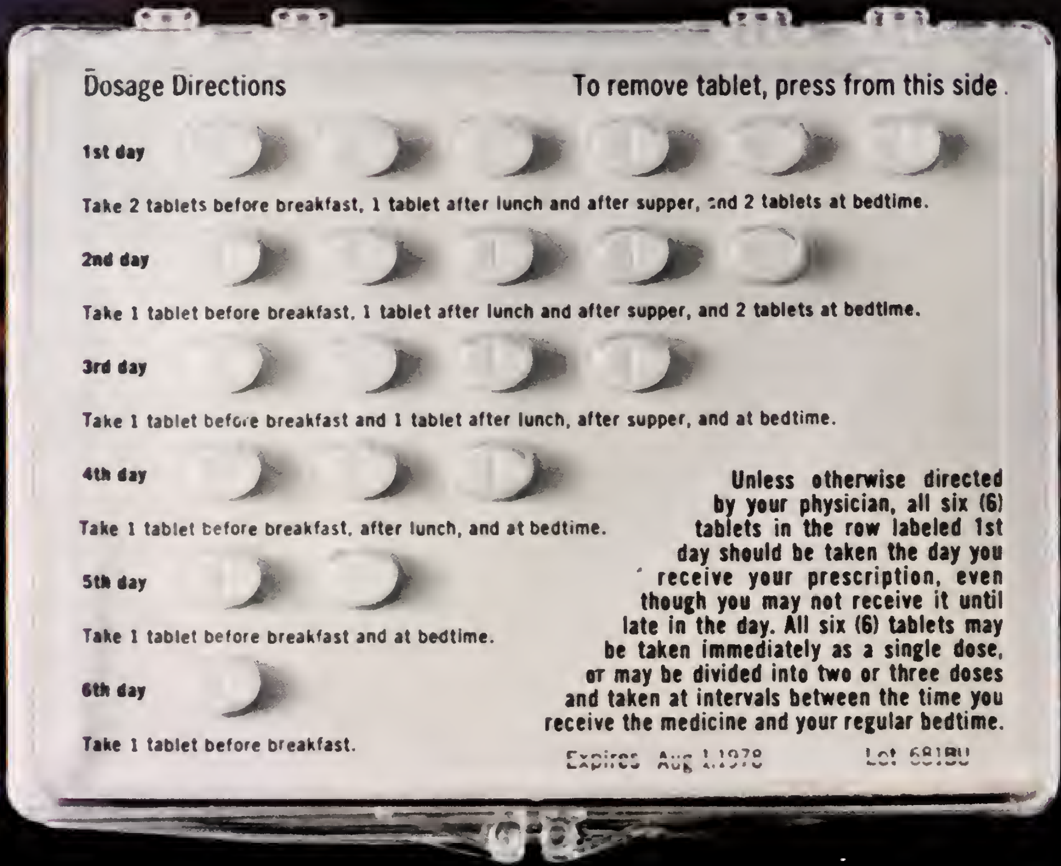

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3rd day

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5th day

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pplementation is of particular importance). Congenital adrenal hyperplasia; nonsup-
rative thyroiditis; hypercalcemia associated with cancer. 2. **Rheumatic Disorders:** As
junctive therapy for short-term administration (to tide the patient over an acute epi-
de or exacerbation) in: psoriatic arthritis; rheumatoid arthritis (selected cases may
quire low-dose maintenance therapy); ankylosing spondylitis; acute and subacute
rsitis; acute nonspecific tenosynovitis; acute gouty arthritis. 3. **Collagen Diseases:**
uring an exacerbation or as maintenance therapy in selected cases of—Systemic
pus erythematosus; acute rheumatic carditis. 4. **Dermatologic Diseases:**
mphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-
hnson syndrome); exfoliative dermatitis; mycosis fungoides; severe psoriasis. 5.
llergic States: Control of severe or incapacitating allergic conditions intractable to
lequate trials of conventional treatment: Seasonal or perennial allergic rhinitis; bron-
ial asthma; contact dermatitis; atopic dermatitis; serum sickness. 6. **Ophthalmic**
iseases: Severe acute and chronic allergic and inflammatory processes involving the
e and its adnexa such as—allergic corneal marginal ulcers; herpes zoster ophthal-
icus; anterior segment inflammation; diffuse posterior uveitis and choroiditis; sympa-
etic ophthalmia; allergic conjunctivitis; keratitis; chorioretinitis; optic neuritis; iritis
d iridocyclitis. 7. **Respiratory Diseases:** Symptomatic sarcoidosis; Loeffler's syn-
rome not manageable by other means; berylliosis; fulminating or disseminated pulmo-
ary tuberculosis when concurrently accompanied by appropriate antituberculous
hemotherapy. 8. **Hematologic Disorders:** Idiopathic and secondary thrombocytopenia
adults; acquired (autoimmune) hemolytic anemia; erythroblastopenia (RBC anemia);
ongenital (erythroid) hyperplastic anemia. 9. **Neoplastic Diseases:** For palliative man-
gement of: leukemias and lymphomas in adults; acute leukemia of childhood. 10.
dematous States: To induce a diuresis or remission of proteinuria in the nephrotic
yndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.
1. **Miscellaneous:** Tuberculous meningitis with subarachnoid block or impending
lock when concurrently accompanied by appropriate antituberculous chemotherapy.
ystemic dermatomyositis (polymyositis).

ONTRAINDICATIONS: Systemic fungal infections.

ARNINGS: In patients on corticosteroid therapy subjected to unusual stress, in-
reased dosage of rapidly acting corticosteroids before, during, and after the stressful
ituation is indicated.

Corticosteroids may mask some signs of infection and new infections may appear
uring their use. There may also be decreased resistance and inability to localize infec-
on. Prolonged use may enhance the establishment of secondary ocular infections due
fungi or viruses.

Since adequate human reproductive studies have not been done, the use in preg-
ancy, nursing mothers or women of childbearing potential requires that the possible
enefits be weighed against the potential hazards to the mother and the embryo or
etus. Infants should be observed for signs of hypoadrenalism.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood
ressure, salt and water retention, and increased excretion of potassium. These effects
re less likely to occur with the synthetic derivatives except when used in large doses.
ietary salt restriction and potassium supplementation may be necessary. All corticos-
eroids increase calcium excretion.

While on corticosteroid therapy, patients should not be vaccinated against small-
ox. Other immunization procedures should not be undertaken in patients who are
n corticosteroids, especially on high dose, because of possible hazards of neuro-
ogical complications and a lack of antibody response.

The use of corticosteroids in active tuberculosis should be restricted to those cases
of fulminating or disseminated tuberculosis in which the corticosteroid is used for the
management of the disease in conjunction with an appropriate antituberculous regi-
men.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

PRECAUTIONS: Hormone therapy is an adjunct to, and not a replacement for, conventional therapy.

Dosage should be individualized according to the severity of the disease and the response of the patient. As soon as a satisfactory clinical response is obtained, the daily dose should be reduced, either to termination of treatment or to the minimal effective maintenance dose level. The lowest possible dose should be used and when reduction in dosage is possible, the reduction should be gradual if the drug has been administered for more than a few days. If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Psychic derangements may appear or existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia..

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Blood pressure, body weight, routine laboratory studies, including 2-hour postprandial blood glucose and serum potassium, and a chest X-ray should be obtained at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with known or suspected peptic ulcer disease.

ADVERSE REACTIONS: Fluid and Electrolyte Disturbances. Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension. **Musculoskeletal.** Muscle weakness; steroid myopathy; loss of muscle mass; osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones. **Gastrointestinal.** Peptic ulcer with possible perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis. **Dermatologic.** Impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating. May suppress reactions to skin tests. **Neurological.** Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment. Convulsions; vertigo; headache. **Endocrine.** Development of Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; menstrual irregularities; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; increased requirements for insulin or oral hypoglycemic agents in diabetics. **Ophthalmic.** Posterior subcapsular cataracts; increased intraocular pressure; glaucoma; exophthalmos. **Metabolic.** Negative nitrogen balance due to protein catabolism.

DOSAGE AND ADMINISTRATION: The initial dosage may vary from 4 to 48 mg per day. **Requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient.** The proper maintenance dosage should be determined by decreasing the initial dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

ALTERNATE-DAY THERAPY (ADT): ADT is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects including pituitary-adrenal suppression, the Cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

Medrol (methylprednisolone) or other short-acting (producing adrenocortical suppression for 1¼ to 1½ days following a single dose) corticoids are recommended for ADT. Complete control of symptoms will not be possible in all patients. When considering this mode of therapy, keep in mind the basic principles and indications for corticosteroid therapy. The benefits of ADT should not encourage the indiscriminate use of steroids.

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Indications: *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. **Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Your Priority?

THE CURRENT ECONOMY has required reassessment of the operations and activities of most governments, industries, businesses, and households. Medical societies are no exception. In fact, like governments, their problems are intensified because not only are their cost of operations increasing, but also their commitments are burgeoning. Obviously, these problems of the economy involve the operation of our medical journals. In truth, before the recession, the Postal Reorganizational Act of 1970 had publications in trouble, the staggering increase in mail rates having already scuttled *Look, Life,* and several lesser magazines. There are too many legitimate demands upon the dues dollars of medical societies. What are the priorities?

We believe the investment in your medical journal has been a good one. Over the years the small amount of dues of the member for his journal subscription has produced proportionately more dividends than the huge sums spent for other things. We repeat (RMMJ, Jan. 1975), we have supported and participated in expenditures past and present to stave off socialized medicine. However, the fact is that in the relentless effort of government to take over control of medical practice *our scientific powerbase is our strongest asset.* It always has been, and always will be. The scientific learning of the physician, with its steady expansion, is our reason for being, and, likewise, our only hope of surviving. Our excursions into government, politics, economics, and social welfare are based upon our unique position as medical scientists in the scheme of democracy. Our impact in these arenas is directly proportional to our scientific strength.

Professional scientific journals are the backbone of medical science. Advancement of the science is the only reason for journals to exist. They cannot be replaced by the throw-aways, regardless of their sometimes high caliber. In the gradual invasion of government into medicine there has been no encroachment into the activities of the professional publications. We submit that the scientific journal may become increasingly important as our independence is slowly eroded by government intervention — it may be the last thing we can call our own.

To serve its readership, the *Rocky Mountain Medical Journal* must be a non-specialty journal. Admittedly this type of journal is less appealing to many physicians than their specialty publications. However, we think there is a place for a journal which covers all aspects of medicine, and we suggest that the physician who thinks he needs only his specialty magazine is copping out. Why should not a doctor make an effort to retain the broad knowledge of medicine which he had when he was graduated from medical school? Certainly, seeming disdain for this overall knowledge of medicine has damaged our public image.

As a non-specialty journal we will take second place to only *JAMA* and the *New England Journal of Medicine.* We are proud of many of our original papers and their world-wide readership as evidenced by requests for reprints. We think it is extremely important that, regardless of the size of his community, the physician has an opportunity to publish an interesting case report — important for him and for his peers. We are pleased with the appearance of the covers of the *Rocky Mountain Medical Journal,* the western motif, the seasonal scenes, and the Russell prints. We like the special issues of the different state societies. We are interested in the medical scientific activities of the *whole* Rocky Mountain area.

But — these are opinions, subject to the natural bias of people who believe in what they are doing. The real purpose of this editorial is to encourage you, the reader, to participate in the readership survey being conducted in this issue. Please fill in and mail the postcard enclosed on the insert in the front portion of the *Journal.* We don't think you are going to get back the six dollars of your dues money that goes for the *Journal,* but we are interested to know if you think there is a better way for your Society to spend it. You have heard our arguments. Let us have your answers and suggestions.

Publication rules and suggestions to authors

1. Who may submit articles. The Rocky Mountain Medical Journal ordinarily accepts only articles prepared by members of the state societies we serve and by guest speakers at their official meetings.

2. Method of preparation. All material for publication must be typewritten, double spaced, with liberal margins, using only one side of the paper, pages consecutively numbered, and preferably on standard 8½ x 11 white bond paper. Carbon copies are *not* acceptable.

Title (preferably short) and author's name, city and state must appear at the top of the first page. Second and subsequent pages should be identified with consecutive page numbers and author's surname. If physician authors possess more than one degree, the MD only is used. Lesser degrees of non-MD authors or co-authors may be used.

Please include beneath the title or at the top of the first page a brief paragraph stating what the article is designed to show and, therefore, why it should be read. This introductory feature is, in editorial parlance, called the "blurb"; it is printed in bold type.

3. Where to submit material. All copy must be sent to the editor for the state in which the material originates. Editors for each state, with their mailing addresses, are listed monthly on the Table of Contents page of the Journal.

4. Acceptance or rejection. The state editor will (1) tentatively accept the article, (2) return it to the author with suggestions for revision, or (3) reject it. He will edit and forward approved copy to the publication office in Denver for final editing and scheduling.

5. Order of publication. Ordinarily, articles will be published in the order received. Those whose value is seasonal, whose value would be lost if publication is delayed, or which reflect priority of original research, are given special consideration. State presidential addresses, programs, state society minutes, and timely organization· announcements are given priority.

6. Length of articles. Scientific papers should be "boiled down" not to exceed ten pages of double-spaced typewritten standard 8½ x 11 inch sheets. Shorter papers are more acceptable to editors and readers, and earlier publication is probable. Every journal is in competition for the reader's time, and condensation is the order of the day. For this reason, and because of financial and space limitations, we request that copy be condensed to the greatest extent consistent with conveying the message.

7. Illustrations. A limited number of illustrations or "cuts," usually up to six, will ordinarily be accepted within our own publication budget if the editor believes they enhance the value of the article. Clear photos, simple diagrams or line drawings in black on white, printing rather than writing, reproduce well. Cuts should be mounted separately, and the paper or cardboard mounts should be the same size as that upon which the article is typed. Each should have its caption below: Fig. 1, Fig. 2, etc., with a short descriptive sentence. Authors will be billed our cost for excess above six cuts.

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9. Case reports. Case reports are popular with our readers. A brief introductory statement concerning the condition or disease, tells why the case is presented. The report follows with a separate heading, CASE REPORT or CASE 1, CASE 2, etc. Include only relevant, positive laboratory and other data. Names, initials, and numbers are unimportant; age, sex, and sometimes occupation are significant. Minimize dates; then make it month, date, year–as February 9, 1969; not 2/9/69. After the case presentation, review or sum it up under a heading such as Discussion, Comment, Summary or Conclusion.

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11. References. Reference lists rarely add to the value of an article for the majority of readers. We will make every effort to publish short reference lists, but long ones will be deleted. Incidentally, the proper heading is "References," not "Bibliography." The latter implies everything in the literature upon the subject. Make them uniform in style and brief, as: Jones, W. K.: Pyelonephritis in Infancy. JAMA 141:75. 1964.

12. Editorials. We would like to have more submitted by our State editors and the membership at large. Readers must get tired of thunder from publication headquarters in Denver; frankly, we do too! Speak out, and we'll sign your name, initials, or respect your request for anonymity, as you choose. If you don't like something we do or say, please let us in on it; we could even stand to hear about it if something happens to please you. A "Letter to the Editor" may help you get something off your mind. We're asking for it and we have a place to put it–in the Journal, that is!

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Horizontal flow clean room*

Bacteriologic studies

**J. Phillip Nelson, MD, Alba R. Glassburn, Jr., MD,
Richard D. Talbott, MD and James P. McElhinney, MD, Denver**

The importance of airborne bacteria in etiology of deep clean wound infection, particularly after implantation of foreign material as in major joint replacement, has received increasing attention. This paper reports efforts to reduce this source of contamination.

Deep wound infection following implantation of large amounts of foreign material is often a serious complication which may cause failure of the operative procedure. Efforts to reduce the rate of deep wound infection must be predicated on an understanding of the pathogenesis of post-operative sepsis in clean wounds. That the presence of foreign material in a wound potentiates development of infection and impedes treatment of an established infection is well accepted. Burke[1] has shown that all clean large wounds are contaminated at the end of an operative procedure. Clean wound bacterial contamination and therefore possible infection occurs from two sources. The first source is endogenous from the patient, such as from bacteremia or from skin. The second is an exogenous source such as breaks in sterile technic or airborne bacterial deposition on sterile surfaces including the wound. It is with this last area of airborne bacterial contamination of wounds and sterile surfaces that this report is concerned.

Airborne bacteria in the operating room air are derived almost entirely from people in the operating room. People shed bacteria into the environment at rates ranging from 3,000 to 50,000 per minute dependent on their activity levels and the effectiveness of their garment barriers[6]. These shed bacteria are found in the air agglomerated to particles of non-viable matter, usually greater than 2 microns in size.[5] Almost all exfoliated bacteria are gram positive organisms.[4] Gram negative enteric bacteria are rarely found in the air. Most airborne bacteria originate from the skin and not from the nasopharynx except when there has been explosive breathing. Each person has a relatively constant rate of bacterial shedding, and a few individuals may persistently shed extraordinarily large amounts of a certain type of bacteria. These individuals are known as shedders as opposed to carriers who do not disperse into the air large numbers of a certain type of bacteria despite its presence on body surfaces.

Since it is difficult, if not impossible, to reduce the amount of bacterial shedding at its source, the control of these organisms in the operating room air must then lie in preventing them from reaching the air and, if they do reach the air, in washing them away from sterile surfaces rapidly. These goals may be achieved by utilizing more efficient barrier garments, helmet aspirator systems, and the Clean Room.

Cotton cloth traditionally used in the construction of operating room gowns has pore sizes in excess of 50 microns. Their effect on preventing shed particles and bacteria from the body from getting into the air has been likened to the effect of a tennis fence on a BB-shot.

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TABLE 1
AIRBORNE BACTERIA SAMPLING AT WOUND

Room Type	Garment	Procedure**	(No.)	Bact./ Cu. Ft.
STANDARD O.R.	Cotton	Hip Nail - Prosthesis	(6)	3.87
CLEAN ROOM	Cotton	Total Hip	(30)	.84
CLEAN ROOM	H-A-P*	Total Hip	(14)	.11
CLEAN ROOM	Cotton	Total Knee	(2)	.56
CLEAN ROOM	H-A-P	Total Knee	(11)	.48
CLEAN ROOM	Cotton	Total Hip and Knee	(32)	.84
CLEAN ROOM	H-A-P	Total Hip and Knee	(25)	.27

* Helmet-Aspirator-Paper Gown
** Approximately 50 cubic feet of air sampled per case.

Furthermore, when cotton becomes wet, the passage of bacteria from the internal to the external surface of the gown is enhanced. Newer materials, such as finely woven cotton, reinforced papers and synthetic woven plastic materials have much smaller pore sizes and thereby definitely impede shedding.[2]

The helmet aspirator system when combined with more impermeable gown material allows the evacuation of trapped bacterial laden air from between the gown-body space. Furthermore, it also evacuates bacteria originating from the head and cools the individual wearing the system by promoting evaporation.

A Clean Room is any area in which airborne particles, including bacteria, are controlled. A laminar air flow Clean[8] Room is characterized by the following features: (1) Blower system and chamber (plenum) for pressurization, (2) HEPA filters lining one surface of the plenum, and (3) Walls to keep air movement directional. In most laminar flow Clean Rooms, the fan speed is adjusted so as to create an air speed in the enclosed space of 80 feet per minute. This causes an air exchange rate of 480 times per hour in a 10 foot long enclosure. The HEPA filters used in most laminar flow Clean Rooms have an efficiency of 99.97% for particles 0.3 microns in size or larger. Class 100[3] conditions are produced at the filter bank consisting of fewer than 100 particles 0.5 microns or larger in size per cubic foot. Since bacteria are greater than 0.3 micron in size and since most airborne bacteria reside on particles greater than 2 microns in size, the air emitted from the filter bank is sterile. The relatively rapid turnover of air in the enclosure washes out essentially all bacteria which may penetrate the helmet-aspirator-paper gown system.

The purpose of this report is to summarize our experiences with surface and airborne bacterial contamination in a Horizontal Flow Clean Room using a standard helmet-aspirator-paper gown system. Portions of this report have recently been published in Orthopedic Review.[7]

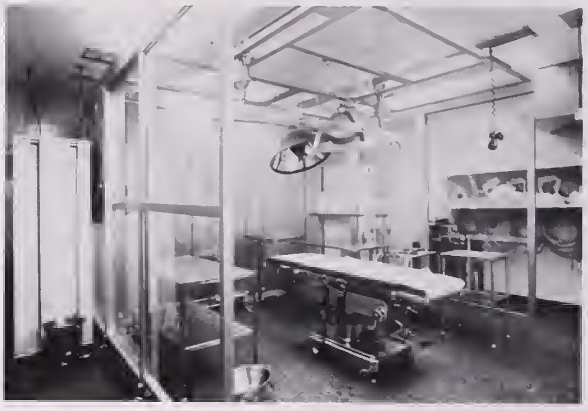

Fig. 1. Horizontal flow Clean Room.

Airborne Bacterial Concentrations

All airborne bacterial sampling was done with a gelatine membrane sampler. The sampler head was located within six inches of the wound and air was sampled at the rate of one cubic foot per minute. The cellulose membranes were plated on blood agar and read at 48 hours.

The regular operating room studied was 18′ x 18′, approximately five years old, and had approximately 14 air exchanges per hour through 95 per cent efficient filters. Regular gowns were cotton muslin with fiberglass masks and hoods. The Clean Room was a horizontal flow Class 100 module with dimensions of 10′ x - 10′ installed in the existing operating room (Fig. 1). The experimental helmet-aspirator-paper gown system (H-A-P) consisted of a plexiglass bubble helmet with aspirator and paper gown (Fig. 2 and 3).

Sampling with the membrane sampler at various areas in a regular operating room produced counts varying from 2.66 to 6.87 bacteria per cubic foot (94.3 to 243.9 bacteria per cubic meter) with an average of 4.76 per cubic foot (169.0 per cubic meter). Table 1 summarizes our experience for various procedures using different combinations of environments and garmenting. These data indicate an approximate five-fold decrease in the number of airborne bacteria using the Clean Room and standard cotton garments. When the helmet-aspirator-paper gown system was utilized, the number of airborne bacteria at the wound was reduced by over thirty-five times for total hip operations and fourteen times for total hip and total knee

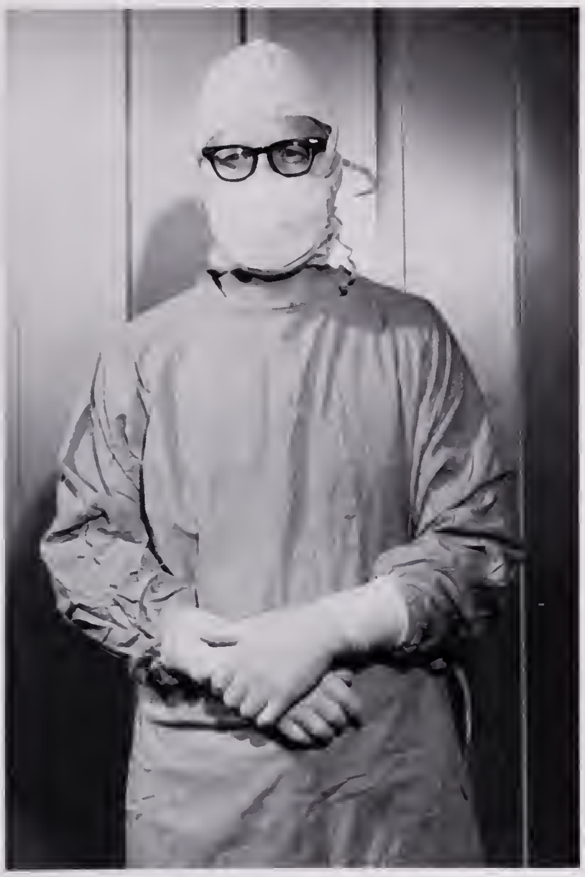

Fig. 2. Standard cotton gown and fiberglass mask and hood garmenting.

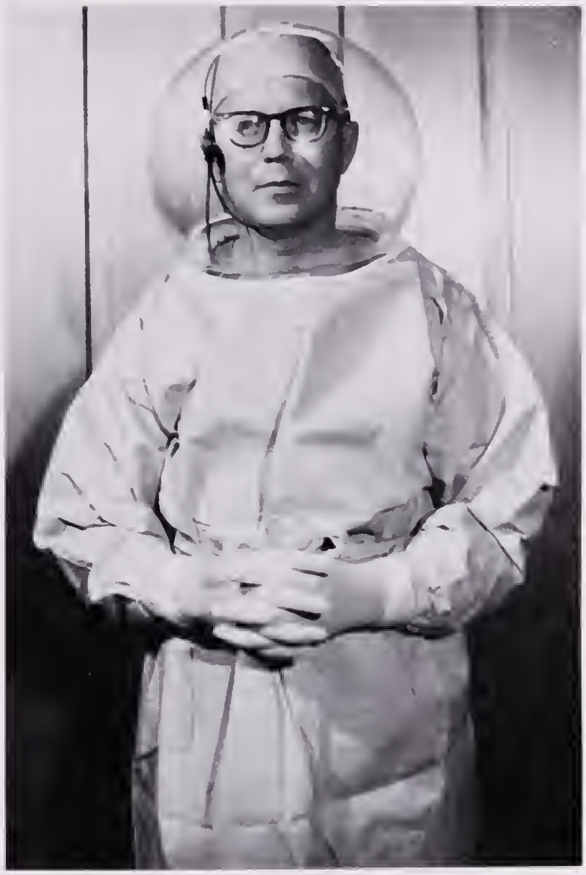

Fig. 3. Helmet-aspirator-paper gown garmenting.

operations combined. These differences are statistically highly significant. The types of bacteria isolated were almost entirely gram positive cocci with Staph epidermitis, Diphtheroids, and Micrococcus predominating. Staph. aureus and fungi were rarely isolated.

Bacterial Surface Sampling

Results of clean wound cultures taken within 20 minutes of incision with a swab and then plated on blood agar and immersed in thioglycolate broth are tabulated in Table 2. The cultures were obtained in the regular operating room with cotton gowns, the Clean Room with cotton gowns and the Clean Room with the helmet-aspirator-paper gown system. There is a four-fold decrease in the rate of contamination from the regular operating room to the Clean Room operating room—a statistically significant difference. When the helmet-aspirator-paper gown system was used, a further decrease in wound contamination occurred but was not statistically significant. There is no significant difference between the contamination rates for the total study of clean wounds and the rates for just the total hip and knee replacements. This data is interpreted to mean that a significant portion of clean wound contamination is derived from airborne bacteria and that by reducing the number of bacteria in the air, a substantial reduction in wound bacterial contamination can be effected.

Agar contact plates were used to determine contamination rates at the conclusion of operative procedures of surgical gloves and surgical drapes in the Clean Room with cotton garments and with the helmet-aspirator-paper gown system. These results are contained in Table 3. Despite the use of the Clean Room, at least 20 per cent of gloves and drapes were contaminated with standard garments, but when the helmet-aspirator-paper gown system was used, contamination rates were substantially reduced. It is concluded that by reducing airborne bacterial concentrations and improving personnel barrier systems, surface contamination may be substantially reduced.

TABLE 2

WOUND BACTERIAL CONTAMINATION RATES

Room and Garment	Site of Culture	No. of Cases	No. of Cultures	Positive Cultures	Contamination Rate (%)
REGULAR O.R. COTTON	SUPERFICIAL	56	56	10	17.9
	DEEP	107	107	25	23.4
	OTHER	14	14	4	28.6
	OVER-ALL	108	177	39	22.0
CLEAN ROOM COTTON	SUPERFICIAL	344	344	16	4.7
	DEEP	551	556	32	5.8
	OTHER	27	29	1	3.5
	OVER-ALL	590	929	49	5.3
CLEAN ROOM H-A-P	SUPERFICIAL	107	107	1	.9
	DEEP	120	120	4	3.3
	OTHER	18	21	2	9.5
	OVER-ALL	122	248	7	2.8

TABLE 3

MICROBIAL SAMPLING OF SURGICAL GLOVES AND DRAPES IN A CLEAN ROOM

Surface	System	No. Operations	No. Samples	% Positive
GLOVES	Cotton	22	98	20
	H-A-P	31	180	3.2
DRAPES	Cotton	57	57	23
	H-A-P	36	36	8.3

Summary

Increasing attention has recently been focused on the part airborne bacteria may play in the etiology of deep, clean wound, post-operative sepsis, particularly after implantation of large amounts of foreign material such as in major joint total replacement. This paper reports our efforts to reduce airborne bacterial concentrations by comparing airborne and sterile surface contamination in a regular operating room and Clean Room operating room with personnel using standard garmenting and a helmet-aspirator-paper gown system. Airborne bacterial concentrations and sterile surface contamination are significantly reduced in the Clean Room environment and these parameters are further reduced using improved personnel barrier technics.

Whether the bacteria responsible for infection of clean deep surgical wounds originate from endogenous or exogenous sources is still controversial. However, the present study appears to demonstrate conclusively that by reducing operating room airborne bacteria, using a Clean Room and a more efficient personnel barrier system, substantial reductions in wound and sterile surface bacterial contamination can be achieved. Logic would seem to dictate that this is a desirable step in the further control and eventual eradication of clean deep wound infections.

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Measles-mumps-rubella vaccine*

Advance in immunization

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As immunization practices evolve and new technology is developed, it is imperative for the practicing clinician to keep abreast of this field.

Active immunization and routine evaluation stand as the framework of pediatric practice today. The effectiveness of active immunization is clearly demonstrated by the success of smallpox eradication programs worldwide and the forecasts that smallpox will be eradicated as a health hazard during the 1970's. Similarly polio and diphtheria-pertussis-tetanus immunizations in the United States have produced significant reductions in morbidity and mortality. These reductions are reflected in morbidity data compiled by the Center for Disease Control, noting only 5 cases of polio in 1974, 257 of diphtheria, 94 of tetanus, and 1758 of pertussis. No reported cases of smallpox have occurred in the United States since 1949.[1] A major step in the last decade has been the introduction of live attenuated virus vaccines against three significant childhood diseases—measles, mumps, and rubella.

The development of combined, trivalent measles-mumps-rubella vaccines promises to be an important breakthrough in control of these diseases in the United States. However, it is clear that based upon previous uncertainties about the simultaneous administration of multiple live virus vaccines, that extensive field studies were required prior to licensure. The trivalent vaccine had to provide equivalent seroconversion without an exacerbation of side effects. This paper will summarize the data that led the United States Public Health Service Advisory Committee on Immunization Practices and the Committee of Infectious Diseases of the American Academy of Pediatrics to develop their current recommendations.[2]

Field studies

Initial vaccine field trials combined two of the three licensed vaccines and documented their efficacy as measured by seroconversion. Subsequently measles, mumps, and rubella were combined in extensive field trials looking at seroconversion as well as clinical reactions to the trivalent vaccine. Following the licensure of the trivalent, combined vaccine, additional clinical studies were conducted to document their efficacy in combination with trivalent oral poliomyelitis vaccine. We will deal with these field trials by category to provide some sense of the development of present vaccine recommendations.

A. Measles-Rubella Vaccines

Villarejos et al employed four lots of bivalent Moraten measles and duck embryo rubella vaccine in a field trial of 375 children, 9 months to 8 years of age (mean of 1.8 years), who were initially antibody negative against either virus. Measles seroconversion by hemagglutination inhibition occurred overall in 98.9 per cent of the children and rubella in 95.5 per cent. Fever was noted most frequently during the 5-12 day period following vaccination and no other significant clinical complaints were noted. This was substantiated by a questionnaire completed 6-8 weeks after vaccination which was directed at looking for late sequelae of arthritis or arthralgia. No attempt was made to separate out the seven children who were vaccinated below one year of age.[3]

In 1971 and 1972, the Center for Disease Control administered Schwarz measles and Cendehill rubella vaccines to 408 susceptible children in four cities. The vaccines were given as a combined product or simultaneously at separate sites. Equivalent seroconversion rates were produced when the vaccines were given as the combined product or simultaneously. The levels compared favorably with those of Villarejos, noting seroconversion rates of 90 per cent or better from rubella and measles in all of the groups studied without any significant increase in side effects.[4]

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TABLE 1

Seroconversion Rates and GMTs of
Seronegative Children to Measles-Rubella Vaccine (4)

	Method of Administration	Number of Children	Measles		Rubella	
			Rate	GMT	Rate	GMT
Tol	Combined	197	96%	1:77	93%	1:82
Tampa	Combined	114	94%	1:58	96%	1:25
Miami	Separate	61	97%	1:54	90%	1:24
Norfolk	Separate	36	92%	1:33	94%	1:26
Total		408	95%		94%	

B. Mumps-Rubella Vaccines

Weibel et al investigated a combined duck embryo rubella and Jeryl Lynn mumps vaccine in Pennsylvania and Costa Rica. A total of 415 children aged 7 months to 7 years (mean of 3.4 years) were vaccinated in 1969 with seroconversion rates of 94 per cent and 96 per cent to rubella and mumps, respectively. No significant clinical reactions, including fever, were noted in the 28 days post vaccination. The absence of fever following administration of this vaccine and its presence in the measles-rubella vaccine implies the measles component is the cause of the fever. Again, no effort was made to look at seroconversion rates of children under one year of age.[5]

C. Trivalent Measles-Mumps-Rubella Vaccines

Subsequent to the documentation that the bivalent vaccines produced equivalent seroconversion rates to monovalent vaccines without any adverse effect on clinical reactions attributable to the vaccines, two groups investigated the therapeutic efficacy of a trivalent measles-mumps-rubella vaccine.

Stokes et al working with Hilleman did the most thorough early study which was reported in 1971. A total of 715 children ranging in age from 7 months to 7 years were selected for no prior history of vaccination or illness consistent with rubella, measles, and mumps. This was later serologically confirmed. Careful clinical observations were made in the subsequent 28 days and this was collected at the time of the second bleeding for the convalescent blood. Serologic response in the triple seronegative children was excellent. Seroconversion rates were 96 per cent to measles, 95 per cent to mumps, and 94 per cent to rubella. Clinical findings noted an increase in fevers 5-12 days following vaccination. There was also a somewhat greater occurrence of upper respiratory tract illness among the vaccinees than among the controls. No increased incidence of arthritis or arthralgia was noted.[6] Borgono in Chile also working with Hilleman found similar results in his field trials.[7]

The Center for Disease Control has conducted comparable studies in Houston, Texas, and Guam with similarly encouraging results. During 1970-1972, 186 children in the two sites were vaccinated using the trivalent vaccine. Seroconversion rates were 96 per cent, 92 per cent, and 95 per cent to measles, mumps, and rubella respectively[4] (Table 2).

D. Dosage Variations in Measles-Rubella and Measles-Mumps-Rubella Vaccines

Although a minimal potency is required by the Bureau of Biologics for any lot of vaccine that is released in the United States, there is a range in the virus titers in the vaccines that are released for general use. Initially concern was expressed that a suppression of the immunologic response would occur should a licensed vaccine have a "high dose" component (high virus titer) and a relatively "low dose" of another component, although still within the potency requirements defined by the Department of Health, Education, and Welfare.

TABLE 2

Seroconversion Rates of Seronegative Children
To Measles-Mumps-Rubella Vaccine With and Without
Polio Vaccine in Two Studies (4)

		Measles		Mumps		Rubella	
Study	Vaccine	No. of Children	Rate	No. of Children	Rate	No. of Children	Rate
Guam	M-M-R	106	100%	82	89%	107	99%
	M-M-R+P	44	100%	42	95%	45	98%
Houston	M-M-R	80	91%	80	95%	80	89%
	M-M-R+P	78	97%	78	94%	78	91%
Total	M-M-R	186	96%	162	92%	187	95%
	M-M-R+P	122	98%	120	94%	123	94%

Two studies were done to evaluate the problems related to variable virus titers. In 1971, Landrigan studied 197 children in Truk who were susceptible to both measles and rubella using various "dosages" of measles and rubella and documented no significant variation in seroconversion rates.[8] A later study in Guam demonstrated similar findings using variable component titers for measles, mumps, and rubella vaccines. Although the rate of seroconversion for mumps was slightly lower than expected, there was no evidence of suppression of immunologic responses to the components of the mumps vaccine in any of the dosage groups.[4]

E. Co-Administration Booster Dose of Vaccine

With the development of the trivalent vaccine, the next obvious question was whether these new vaccines could be co-administered with the trivalent oral poliomyelitis booster vaccine, thereby reducing the mandatory number of well child visits. Again, the Center for Disease Control studied a total of 122 children in Guam and Houston giving the measles-mumps-rubella vaccine in combination with the third booster dose of trivalent oral poliomyelitis vaccine—a total of six antigens. The rates were almost identical for each antigen whether given alone or simultaneously with trivalent polio vaccine.[4] Furthermore the Center for Disease Control documented that the antibody response to all three types of poliovirus were similar in the groups given the booster doses with or without the combined measles-mumps-rubella vaccine. No increase in the frequency or severity of clinical reactions was noted in the Center for Disease Control study groups.[4] (Table 2)

Immunization Recommendations

According to the current guidelines of the United States Advisory Committee on Immunization Practices and the Committee of Infectious Diseases of the American Academy of Pediatrics, measles, rubella, and mumps vaccine should be given after the first birthday either as the combined trivalent vaccine or as a series of monovalent vaccines. Certain exceptions are made to this recommendation, most specifically in the face of epidemic or high endemic levels of measles, where the monovalent vaccine should be given earlier with revaccination at one year of age.[2]

Specific recommendations have developed concerning the use of combined bivalent or trivalent vaccines:

1. They are recommended for primary immunization at one year of age.
2. Measles and rubella vaccines and the third dose of oral trivalent poliomyelitis vaccine may be administered simultaneously during the second year of life.
3. Schwarz measles and Cendehhill rubella vaccines may be given simultaneously at separate sites.

Further studies should investigate the feasibility of giving trivalent vaccine with the booster DPT vaccination. The combined vaccine is not advised for children under one year of age nor for pregnant or immunologically deficient individuals.

Discussion

The development of measles-mumps-rubella vaccines has provided a new tool in preventive pediatrics. Despite the availability of effective vaccines, measles and rubella have continued to be a health threat in the United States and hopefully the multivalent vaccines will expedite the immunization of larger groups of children.

Following the licensure of measles vaccines in 1963, morbidity decreased significantly. By 1968, only 22,000 cases were reported, down from nearly 500,000 cases reported each year prior to 1963. However, a resurgence was noted in 1969 because of shifts in national public health priorities toward rubella programs, resulting in over 75,000 cases in 1971. This trend was reversed in 1972 when large scale efforts were redirected toward the use of the measles-rubella vaccine; not until 1974 was the level of control first reached in 1968 again achieved.

It is particularly relevant to emphasize the need for intensive immunization programs built upon the philosophy of routine rather than sporadic and crisis programs. Immunization levels in the United States have deteriorated in the last few years as documented by data compiled by the Center for Disease Control through the annual Immunization Survey. In 1973, protection by infection and/or vaccine fell from 66.0 per cent to 64.1 per cent for measles and 63.3 per cent to 62.4 per cent for rubella in the 1-4 year old age groups.[9]

Less complete information is available concerning mumps because of the smaller risk factors involved. In point of fact, the Public Health Service Advisory Committee on Immunization

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Practices has recommended that "mumps vaccination programs should not take priority over essential community immunization activities."[10] Furthermore, the mumps component of the trivalent vaccine has been less widely used because of the high costs of this component. Massachusetts is the only state currently employing the triple vaccine in statewide programs, although other areas are considering its introduction.[11] Colorado makes it available in public health programs as the monovalent vaccine. As we see the development of competing trivalent vaccines, it is certain that the marginal cost of including the third component will fall.

The bivalent and trivalent vaccines have been established as an important addition to good preventive pediatrics. Although significant questions remain concerning their long term protective effects, the long term side effects, and their efficacy in children under one year of age, they simplify the vaccination of children and assure that multi-disease programs will be established. However, the vaccine is merely a tool to provide protection, and the health care system must assure that adequate delivery mechanisms are developed to make the vaccine available. Trivalent vaccines provide the primary health care provider with a means of providing effective, quick protection for his patients, but the burden remains upon him to assure its delivery to unprotected populations.[12,13]

ACKNOWLEDGEMENT

We are indebted to Drs. John Ott and Monty Roth for their review of the manuscript.

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Vibrio fetus septicemia in Colorado*

Timothy J. Houlihan, MD, Denver and
James R. Wheeler, MD, Greeley, Colorado

The first three known cases in Colorado of septicemia due to vibrio fetus are reported.

VIBRIO FETUS was first discovered as a cause of abortion in sheep and cattle in 1909 by McFadyean and Stockman.[1] In 1947, Vinzent et al.[2] reported the first case of human vibriosis. Since that time human infection has been uncommon with only slightly over fifty cases having been reported. The organism appears to be ubiquitous, having been isolated in Korea,[3] Israel,[4] Europe,[1] and the United States.[5] To our knowledge no cases have been reported in the state of Colorado.

CASE REPORTS

CASE 1: A 77-year-old female presented with the acute onset of fever, chills, and questionable cyanosis. Temperature was 103.8° orally, pulse 100, B.P. 140/90, respirations 28. Her physical examination was otherwise unremarkable for her age. White blood cell count was 13,600 with a shift to the left. Blood cultures grew out a Vibrio fetus which was confirmed by the State Health Department in Denver and CDC in Atlanta, Georgia. She was not treated with any antibiotics, became afebrile within 24 hours, and was discharged.

CASE 2: A 40-year-old male, meat packing supervisor presented with severe left chest and lower abdominal pain of five hours duration. Physical examination showed B.P. 146/92, pulse 76, respirations 24, temperature 100.8°. He was diaphoretic, had a regular sinus rhythm with a grade 2/6 systolic ejection murmur at the left sternal border, and had right upper quadrant tenderness. The white blood cell count was 12,400 with 80 per cent neutrophils. Blood cultures initially showed no growth. His temperature and white blood count continued to rise during the next five days. Blood cultures were repeated, and a Vibrio fetus was isolated and later confirmed by the Colorado State Laboratory. His antibiotic therapy was changed to ampicillin. Immediate improvement resulted, and he was discharged without further problems.

CASE 3: A 43-year-old cook was admitted with recurrent, atypical, left anterior chest pain. Initial evaluation was negative. One week later he developed a fever of unknown origin with temperature elevations to 103° and WBC of 13,000 with 89 per cent neutrophils. Serial blood cultures grew an atypical gram negative rod, later confirmed by the Colorado State Laboratory to be Vibrio fetus, sensitive to all antibiotics tested. He was treated with intravenous ampicillin for 14 days, became afebrile, and was discharged fully recovered.

Discussion

Vibrio fetus has been shown to cause meningitis,[3] septicemia,[4] arthritis,[5] endocarditis,[6] and biliary tract infection[7] in humans. At first, because of its isolation from animals it was thought to be found in those individuals having contact with animals. Later, in those without known contact, it seemed to have some relationship to the elderly and debilitated. More recently, however, these observations have been disputed, as cases have been reported with no known etiologic or predisposing factors.

Fortunately, most such infections are readily sensitive to a wide variety of antibiotics, and recovery is usually complete without any sequel. Diagnosis continues to depend upon the bacteriologic isolation of the organism.

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*Dr. Houlihan is Resident in Surgery, St. Joseph Hospital, Denver. Dr. Wheeler is Attending Surgeon, Weld County General Hospital, Greeley, Colorado. These cases were collected from St. Joseph Hospital, Denver and Weld County General Hospital, Greeley.

Summary

The first three known cases of septicemia from Vibrio fetus in the state of Colorado have been presented. Vibrio fetus is primarily an animal pathogen, occasionally causing human infection. Once the diagnosis has been established, treatment can be easily instituted, and recovery is usually complete.

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Galactorrhea*

What does it mean?

Fred D. Hofeldt, Lt. Colonel, MC,
Robert A. Adler, Major, MC,
Michael J. Boland, Captain, MC,
Marshall B. Block, Major, MC, Denver

Inappropriate lactation in non-puerperal females is frequently encountered in a clinic population. Based upon an understanding of the underlying physiology and pathophysiology, appropriate diagnosis and therapy can be initiated.

NON-PUERPERAL GALACTORRHEA has been recognized since biblical times. It can occur in either sex. Approximately 1800 years ago, the Talmud (Sabbath 53-B) described a man who nursed his child after his wife's death during childbirth. The causes of non-puerperal galactorrhea are numerous, and it occurs frequently in normal females.[1] An understanding of these disorders is related to a basic knowledge of the physiology and pathophysiology of normal and abnormal breast secretions.

As an unstimulated organ, the breast remains quiescent during childhood. With the onset of adolescence and hypothalamic-pituitary-gonadal maturation, breast growth and development occurs in both sexes. In the female, the various Tanner stages of breast development are well recognized. Gynecomastia occurs in most pubertal males with regression after adolescence in the majority of instances. The breast is a hormonally primed organ whose function and maintenance is influenced directly or indirectly by the secretion of the pituitary trophic hormones (prolactin, ACTH, growth hormone, FSH, LH, TSH) by target hormones (thyroxine, estrogens, progesterone, cortisol) and by the peptides, insulin, and placental chorionic gonadotrophin (HCG). It is in this hormonal milieu that alterations in secretion of hormones have resulted in galactorrhea.

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*From the Endocrine Service, Department of Medicine, Fitzsimons Army Medical Center, Denver. Presented in part at the Regional American College of Physicians meeting, Colorado Springs, Colorado, 17 January 1975. The opinions or assertions contained herein are the private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or of the Department of Defense.

Causes

The spectrum of disorders which cause galactorrhea include local mammary lesions, lesions of the thoracic chest wall and thoracic nerves, spinal cord and central nervous system lesions including those of the hypothalamus and pituitary gland. Specific factors in this pathway include the manipulation of the breasts or stimulation of the breasts with tight fitting garments or other compressive items and mammoplasty. Local chest wall lesions such as radical mastectomy, thoracoplasty, thoracotomy, burns, or herpes zoster of the chest wall may result in a local mediated neuroreflex arc and galactorrhea. Involvement of the nerve pathways to the hypothalamus by encephalitis, pseudotumor cerebri, post-pneumoencephalography or spinal cord lesions including syringomyelia, tabes dorsalis, may mediate galactorrhea in the hormonally primed breast. Other CNS diseases as pineal tumors, craniopharyngiomas or granulomatous disease are associated with galactorrhea. Hypothalamic stimulation may occur by tumor or by a number of drugs including the anti-hypertensive agents (Reserpine, Aldomet®), the phenothiazines (Thorazine®, Stelazine®, Compazine®, Prolixin®, Mellaril®), Meprobamate, the tricyclic antidepressants (Tofranil®), oral contraceptives, and estrogenic steroids. Pituitary involvement with pituitary tumor or section of the pituitary stalk is associated with galactorrhea. Thyroid dysfunction, including hypothyroidism[2] and hyperthyroidism may cause galactorrhea. The majority of patients, however, with galactorrhea generally fall into the idiopathic variety which includes Chiari-Frommel syndrome (galactorrhea-amenorrhea in postpartum patients), the Argonz-delCastillo syndrome (galactorrhea-amenorrhea in nulliparous patients), and the syndrome of isolated idiopathic galactorrhea with normal menstrual periods.

Workup

A careful physical examination of the breast may be needed in many instances to detect subtle inapparent galactorrhea. This can be accomplished by careful circumferential compression of ductal breast tissue towards the nipple and a gentle rolling of the nipple between the thumb and index finger. Such a meticulous examination needs to be conducted in all patients with pituitary tumor as inapparent lactation may be detected. Interestingly, prolactin levels may be elevated in many patients with hypothalamic or pituitary tumors but lactation may not be present in all.[3]

Prior to initiating an extensive evaluation of inappropriate lactation, one should confirm the presence of galactorrhea. In the majority of instances, breast secretions are identified as "milk" on the basis of their characteristic appearance and only rarely has their identity been proven by appropriate analysis. Analysis of these secretions for nitrogen, triglyceride, or cholesterol content or the presence of fat globules may give supportive information in confirming the diagnosis of galactorrhea. We have recently employed a thin paper chromatography method[4] for determining lactose in breast secretions to establish whether bona fide galactorrhea is present. Lactose is the prominent sugar in human milk and within the body is produced only in the breast. If the breast secretion contains lactose, it is milk as chemically defined irrespective of the presence or absence of other components. In a previous study of ten non-puerperal, lactating patients,[4] we identified lactose in breast secretions of only eight patients. In two whose secretions characteristically appeared milk-like, there was no lactose and it was presumed that their breast discharges were due to localized fibrocystic disease of the breast. In those patients without lactose in their breast secretions, further subsequent detailed metabolic workup need not be conducted. The determination of lactose by thin layer chromatography requires less than one drop of the secretion.

If the patient with inappropriate lactation has normal periods and no evidence of pituitary trophic hormone disturbances with normal skull and visual fields, detailed metabolic examination should be minimal, but the patient should be followed at frequent intervals for the occurrence of other hormonal deficiency syndromes or related abnormalities that may be associated with CNS tumor.[5] In five patients studied with idiopathic isolated galactorrhea with normal menstrual periods,[5] the onset of the galactorrhea occurred postpartum in four. All patients studied had serum prolactin levels well within the normal range.

The presence of visual field abnormalities, abnormal sella, associated deficiency of hypothalamic-pituitary-endorgan hormonal function should lead one to pursue a relatively detailed examination to include arteriograms and pneumoencephalograms. Even if the diagnosis of idiopathic amenorrhea-galactorrhea syndrome or idiopathic isolated galactorrhea with normal menstrual periods is made, these patients should be examined at regular six to twelve month intervals. Patients with idiopathic amenorrhea-galactorrhea syndromes were noted by Dr. Raymond Randall of the Mayo Clinic to later develop serious disease. He noted that eight patients with delCastillo syndrome and five patients with Chiari-Frommel syndrome eventually developed pituitary tumors. In sixteen patients with Forbes-Albright syndrome, the mean interval from onset of galactorrhea to diagnosis of the tumor was 5½ years, with the range being 4 months to 18 years. These observations would caution one to follow these patients closely.

Prolactin values may be elevated in a number of the causes of amenorrhea-galactorrhea syndromes, as reported by Frantz.[6] Elevated levels are frequently seen in patients with hypothalamic or pituitary tumors and lactation need not be present in all.[3] If one is suspicious of pituitary tumor, a serum prolactin level should be determined by radioimmunoassay. Small prolactin-secreting tumors of the pituitary gland can be successfully removed without significant damage to residual pituitary trophic hormone function by transnasal microdissection surgery. In patients with pituitary tumor and elevated prolactin levels, the prolactin serves as a marker of successful therapy or recurrence of the pituitary tumor. Assessment of pituitary tumors by various stimulation and suppression tests have not been helpful. Contrary to the enthusiastic report by Buckman, *et al*[7] that patients with pituitary tumors will show no prolactin suppressibility to oral water loading compared to dramatic suppressibility in normal subjects, studies we have conducted show that normal subjects may not consistently suppress their prolactin levels after water loading.[8] Therefore at this time the best test to differentiate tumor-caused from functional galactorrhea is the measurement of basal serum or plasma prolactin.

Treatment

The therapy of galactorrhea is directed at the etiology whenever possible, especially when the cause is CNS tumor. Local anesthesia to spinal nerves has been reported to be successful only in thoracotomy-induced galactorrhea. One should avoid stimulating processes to breast tissue and nipple. Estrogenic and contraceptive steroids have been used with variable degrees of success. Frequently estrogen withdrawal has been associated with the onset of galactorrhea. L-dopa (500 mg four times a day) may be successful in a number of patients with inappropriate lactation but duration of action is short. A new ergocryptine derivative (CB154) not yet released by the FDA appears to have the greatest benefit in treating these patients. Likewise, beneficial results have been noted with ergonovine (0.2 mg three times daily), an ergot alkaloid with negligibly vasoactive effects.

ACKNOWLEDGEMENT

The authors wish to acknowledge the assistance of Ms. Deborah Longhofer in preparation of the text.

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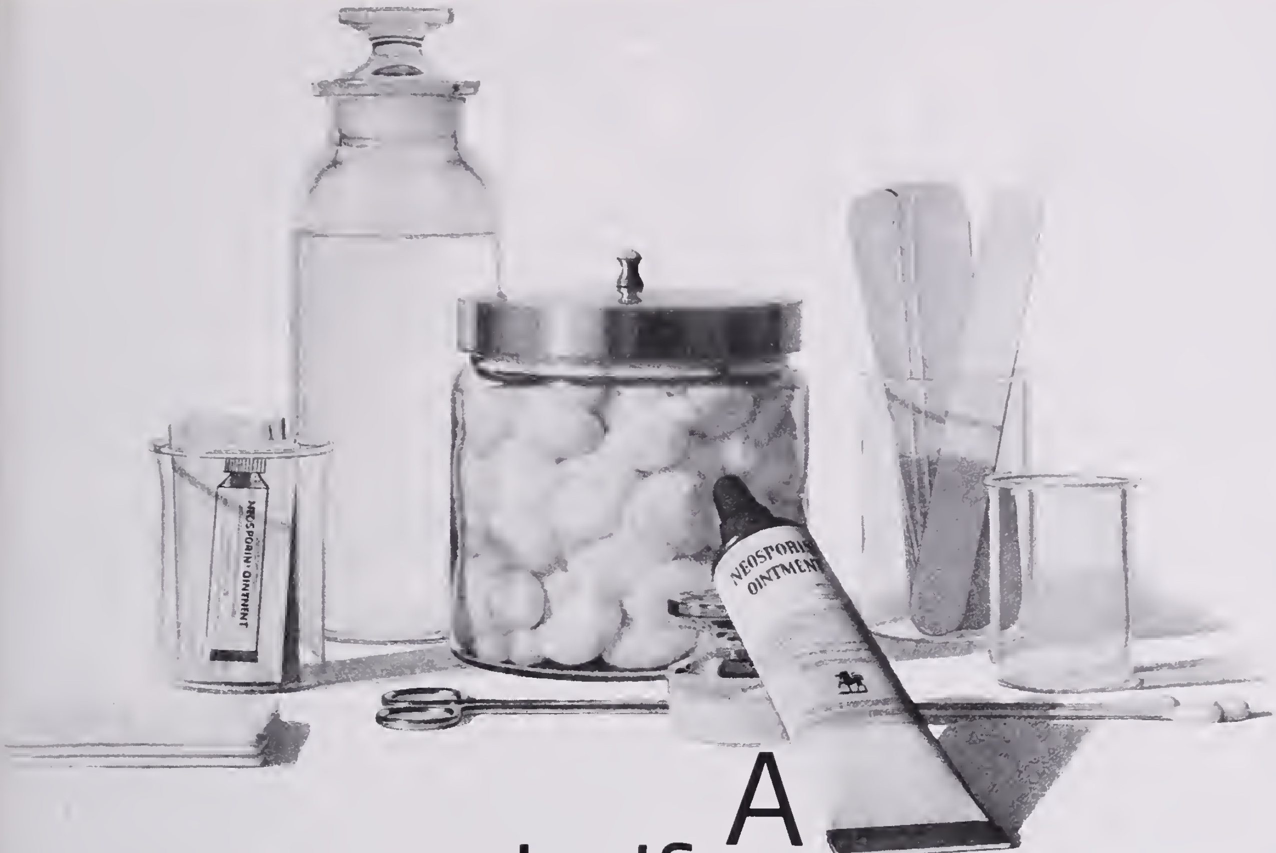

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COLORADO

Colorado State Science Fair

The 1975 Colorado State Science Fair was held April 11-12 at the Cinderella City Shopping Center, Englewood, Colorado. The displays of 148 young Colorado scientists, results of concentrated study and efforts to organize many areas of original research, were open to the public for inspection and analysis.

First Overall winner in the Senior High Group was Kristina Johnson, a senior at Thomas Jefferson High School, Denver, whose "Holographic Study of the Spangiophore of Phycomyces" also ranked First in Senior High Physical Sciences studies. At the International Science and Engineering Fair, held in Oklahoma City May 13 through May 16, Kristina won an Air Force physics award.

First Overall winner in the Junior High Group was Peter Sandborn, ninth-grader at Lesher Junior High School, Fort Collins, whose study of the "Elasticity of Natural Fibers" was judged highly. This work gave him as well the First USAF award for Junior High Physical Sciences as well as the prize for First place in Junior High Physical Sciences.

Mike Mayberry, senior at Fort Morgan High School, Fort Morgan, took Second Overall honors with his demonstration of "Distribution of Prime Twins", which also won him First place in Senior High Mathematics.

Patty Sandborn, eighth-grader at Lesher Junior High School, Fort Collins, took Second Overall honors for her study of "Flying Insects", which also won her honors from the Zonta Club of Boulder, the Rocky Mountain Bioengineering Society, the Society for Technical Communication, the Society of Women Engineers, and also the First place in Junior High Zoology classification.

For her study of "The Effects of Drugs on the Orb-Weaving Spiders", Pamela Pratt, senior at Wasson High School, Colorado Springs, won Third Overall place in the Senior High Division, as well as the First Prize in Senior High Zoology, and an award from the Colorado Psychological Association.

Turning to "Endomorphisms of the Group Obtained by the Rotations of a Tetrahedron", Justin Marble, ninth grader from Arickaree School, Anton, made a display which won him Third Overall place in the Junior High Division, and the U.S. Air Force Award and First place in Junior High Mathematics.

First prize in the category of Senior High Engineering was won by Richard Duszynski, a senior at J. K. Mullen Preparatory School, Denver, for his study of "Utilization and Storage of Solar Energy", which also won for him the Colorado School of Mines Award.

Oran Kanode, junior at Highland High School, Ault, placed first in Senior High Botany for his work on "The Micro World Below Your Feet", which also won him the prize of the Colorado Chapter of the Soil Conservation Society of America.

UTILIZATION AND STORAGE OF SOLAR ENERGY

Richard Duszynski, a senior at the J. K. Mullen Preparatory School, Denver, won first prize in the category of Senior High Engineering for his display on "Utilization and Storage of Solar Energy," for which he also won the Colorado School of Mines Award.

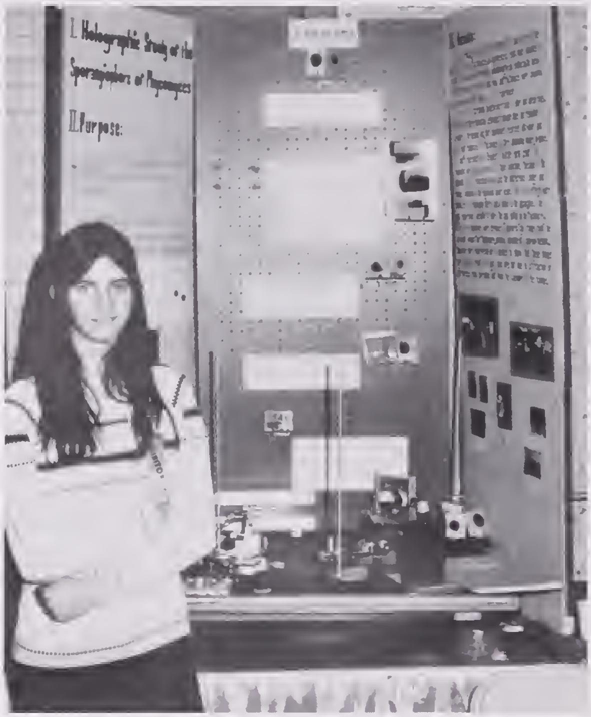
First prize in Junior High Engineering went to J. Austin Garrison, eighth-grader at Lincoln Junior High School, Fort Collins, for his study of the "Effect of Wrinkle Black Surface Treatment on Baseboard Convection," for which he also won U.S. Air Force and U.S. Army commendations.

Gregg Engles, Cherry Creek High School, Arapahoe County, won an Air Force award at the International Science Fair for his exhibit entitled "The Cellular Effects of Indole Acetic Acid and Giberellic Acid on Coleus".

Robert Stamps, tenth grade student at Wasson High School, Colorado Springs, received an award from the U.S. Energy Research and Development Administration for his study of "Power from Plasma".

As in its previous 19 Fairs, the Colorado State Science Fair is sponsored by the Colorado Medical Society; American Cancer Society, Colorado Division; Colorado Engineering Council; National Bureau of Standards; National Oceanic and Atmospheric Administration; Office of Telecommunications/Institute for Telecommunication Sciences; Woman's Auxiliary to the Colorado Medical Society; and The Denver Post. Dr. Sam Shushan served as Fair Director, with Mrs. Eileen Irwin serving as Executive Secretary, and Mrs. Judy Van Zante assisting. Mrs. Betty Whitmore represented the Woman's Auxiliary of the Colorado Medical Society.

A number of academic scholarships were recommended. Kristina Johnson and Pamela Pratt were recommended to the University of Colorado. Richard Duszynski was recommended to Colorado



Kristina Johnson, senior at Denver's Thomas Jefferson High School, is shown by her display entitled "Holographic Study of the Spangiophore of Phycomyces," for which she was named First Overall winner in the Senior High division at the Science Fair.

School of Mines for a $450 scholarship in his first year. Kevin Gertig, Rocky Ford, and Ronald Nickell, Colorado Springs, were recommended to Northeastern Junior College, Sterling.

Tuition waivers of $200 for summer graduate courses at the University of Colorado, Boulder, were made to Mr. Alta Mecham, Fort Collins' Lesher Junior High School, and to Mr. Elvon Gilmore, Thomas Jefferson High School, Denver.

Special acknowledgment should be made to the women's auxiliaries of the Colorado Medical Society and the component societies. These women contributed valuable time in assisting registration, as well as donating funds to the Fair.

The Colorado Medical Society also wishes to thank these component societies who, following House of Delegate instructions, contributed to both their regional science fairs and the state fair, not only in money but by individual effort.

1975 REGULAR SCIENCE FAIR AWARDS

Top Awards — All Exhibits

Junior High
- 1st Place: Peter Sandborn, 9th grade, Lesher Junior High School, Fort Collins, "Elasticity of Natural Fibers"
- 2nd Place: Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, "Flying Insects"
- 3rd Place: Justin Marble, 9th grade, Arickaree School, Anton, "Endomorphisms of the Group Obtained by the Rotations of a Tetrahedron"

Senior High
- 1st Place: Kristina Johnson, 12th grade, Thomas Jefferson High School, Denver, "Holographic Study of the Spangiophore of Phycomyces"
- 2nd Place: Mike Mayberry, 12th grade, Fort Morgan High School, Fort Morgan, "Distribution of Prime Twins"
- 3rd Place: Pamela Pratt, 12th grade, Wasson High School, Colorado Springs, "The Effects of Drugs on the Orb-Weaving Spiders"

Botany Exhibit Awards

Junior High
- 1st Place: Donald Ostwald, 8th grade, Fort Morgan Junior High School, Fort Morgan, "Does Manure Work Better as a Fertilizer if Used in Combinations or if Used Alone?"
- 2nd Place: Greg Lanham, 9th grade, Orchard Mesa Junior High School, Grand Junction, "Waste Not—Want Not"
- 3rd Place: Jim Langin, 7th grade, Walsh High School, Walsh, "Weeds Are Toxic"
- Honorable Mention: Ruth Griswold, 9th grade, Lesher Junior High School, Fort Collins, "A Comparison of Radishes of Fungi in Response to Irradiation"

Senior High
- 1st Place: Oran Kanode, 11th grade, Highland High School, Ault, "The Micro World Below Your Feet"
- 2nd Place: Gregg Engles, 12th grade, Cherry Creek High School, Englewood, "The Cellular Effects of Indole Acetic Acid and Giberellic Acid on Coleus"
- Honorable Mention: Kent McLagan, 12th grade, Cherry Creek High School, Englewood, "Altitudinal Variation in Chlorophyll 'a' Structure in Englemann Spruce"

Engineering Exhibit Awards

Junior High
- 1st Place: J. Austin Garrison, 8th grade, Lincoln Junior High School, Fort Collins, "Effect of Wrinkle Black Surface Treatment on Baseboard Convection"
- 2nd Place: Mark Dean, 8th grade, York Junior High School, Thornton, "Wave Machine (Motion, Construction, and Destruction)"
- 3rd Place: Eric Mogren, 9th grade, Lincoln Junior High School, Fort Collins, "Effect of Dihedral of an Airfoil on the Lift of an Airfoil"

Senior High
- 1st Place: Richard Duszynski, 12th grade, J. K. Mullen Preparatory School, Denver, "Utilization and Storage of Solar Energy"
- 2nd Place: Brian Pearsall, 11th grade, Montrose High School, Montrose, "A Low Cost Mini Computer Terminal"
- 3rd Place: Jack Heidrick, 11th grade, Brush High School, Brush, "The Qualitative and Quantitative Analysis of Underground Streams in Morgan County"
- Honorable Mention: Eric Olsen, 12th grade, Brush High School, Brush, "The Kelvin Water-Drop Generator and the Relationship Between Dipole Moments and Charge Build-up"

Mathematics Exhibit Awards

Junior High

- 1st Place: Justin Marble, 9th grade, Arickaree School, Anton, "Endomorphisms of the Group Obtained by the Rotations of a Tetrahedron"
- 2nd Place: Carl E. Hess, 9th grade, Nevin Platt Junior High School, Boulder, "Fourier Series"
- 3rd Place: Gavin Teague, 8th grade, Josephine Hodgkins Junior High School, Denver, "How to Play Hexapawn"

Senior High

- 1st Place: Mike Mayberry, 12th grade, Fort Morgan High School, Fort Morgan, "Distribution of the Prime Twins"
- 2nd Place: Michael Fox, 12th grade, George Washington High School, Denver, "An Alternate Time Dialation Theory"
- 3rd Place: Joseph Hughes, 12th grade, Wasson High School, Colorado Springs, "Order on a Non-Ordered Field"

Physical Sciences Exhibit Award

Junior High

- 1st Place: Peter Sandborn, 9th grade, Lesher Junior High School, Fort Collins, "Elasticity of Natural Fibers"
- 2nd Place: Lisa Lynn Mallette, 8th grade, Broomfield Junior High School, Broomfield, "Let's Keep It Quiet!"
- 3rd Place: Steven Bender, 9th grade, Wiggins Junior-Senior High School, Wiggins, "Distillation of Beverages"
- Honorable Mention: Diane Bacon, 7th grade, Woodlin School, Woodrow, "Fabric Inflammability"

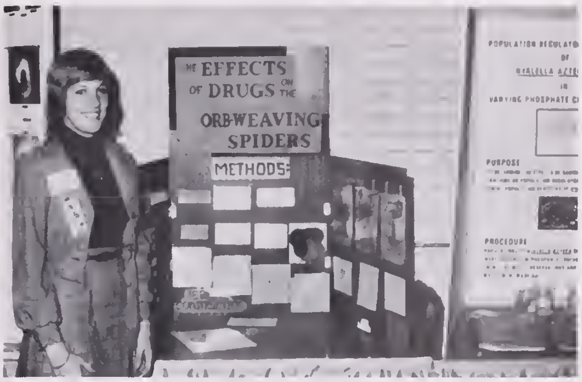
Senior High

- 1st Place: Kristina Johnson, 12th grade, Thomas Jefferson High School, Denver, "Holographic Study of the Sporangiophore of Phycomyces"
- 2nd Place: Rex Craig, 10th grade, Prairie High School, New Raymer, "The Zinc-Ion Laser: Composite Fringe Signal Analysis"
- 3rd Place: Scot Heath, 12th grade, Frenchman RE-3, Fleming, "The Aerodynamics of a Frisbee"
- Honorable Mention: Dave Lovering, 12th grade, Lakewood High School, Lakewood, "Space-Time Curvature and the Propagation of Gravitational Radiation"

Zoology Exhibit Awards

Junior High

- 1st Place: Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, "Flying Insects"
- 2nd Place: Joe Britton, 9th grade, Blevins Junior High School, Fort Collins, "Pharmacology of Conditioning"
- 3rd Place: Gordon Gerson, 7th grade, Air Academy Junior High School, Colorado Springs, "The Effect of Soft Drinks on Teeth"
- Honorable Mention: Carmen Gilbert, 7th grade, Bayfield Junior High School, Bayfield, "In Search of Sinistrals"


THE EFFECTS ON THE DRUGS OF ORB-WEAVING SPIDERS
METHODS

A study of "The Effects of Drugs on the Orb-Weaving Spiders" won for Pamela Pratt Third Overall place in the Senior High division and also the First Prize in Senior High Zoology, as well as an award from the Colorado Psychological Association.

Senior High

- 1st Place: Pamela Pratt, 12th grade, Wasson High School, Colorado Springs, "The Effects of Drugs on the Orb-Weaving Spiders"
- 2nd Place: Richard Russel, 11th grade, St. Mary's High School, Colorado Springs, "Gamma Ray Induced Chromosomal Aberrations in Human Leukocytes"
- 3rd Place: Donald Beard, 10th grade, Hotchkiss High School, Hotchkiss, "Chiromids: Indicators of Pollution"
- Honorable Mention: Ronald Nickell, 12th grade, Coronado High School, Colorado Springs, "The Effect of Methyl and Dimethyl Mercury on Rodents"

Amelia Earhart Award
Zonta Club of Boulder County

Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, "Flying Insects"

American Cancer Society, Colorado Division

Junior High

- Carolyn Wilson, 8th grade, Everitt Junior High School, Wheat Ridge, "What's So Bad About Cigarettes?" (Z)

Senior High

- Richard Russel, 11th grade, St. Mary's High School, Colorado Springs, "Gamma Ray Induced Chromosomal Aberrations in Human Leukocytes" (Z)

American Society for Microbiology

Junior High

- 1st Place: Leslie Ross, 8th grade, Burlington Middle School, Burlington, "A Garlic Gargle?"
- 2nd Place: Kriss Acott, 9th grade, Frenchman RE-3, Fleming, "Does Toothpaste Make a Difference?"
- 3rd Place: Stephen Wright, 7th grade, Clear Lake Junior High School, Denver, "Bread Preservatives: Do They Work?"

Senior High

1st Place: Kristina Johnson, 12th grade, Thomas Jefferson High School, Denver, "Holographic Study of the Sporangiophore of Phycomyces"

2nd Place: Kevin Gertig, 12th grade, Rocky Ford High School, Rocky Ford, "Carbon Limitation in Algal Growth of Effluent as Predicted by Diurnal pH Patterns"

3rd Place: Christine Specht, 12th grade, Poudre High School, Fort Collins, "A Rapid Microbial Technique for Determining the Age of Biological Specimens"

Honorable Mention: Karen Tracy, 10th grade, Poudre High School, Fort Collins, "A Comparison of the Production of Methane and CO_2 from the Production of Animal and Plant Waste"

Boulder Chapter of Sigma Xi

Brian Pearsall, 11th grade, Montrose High School, Montrose, "A Low Cost Mini Computer Terminal"

Colorado Medical Society

Richard Russel, 11th grade, St. Mary's High School, Colorado Springs," Gamma Ray Induced Chromosomal Aberrations in Human Leukocytes"

Colorado Psychological Association

Junior High

Joe Britton, 9th grade, Blevins Junior High School, Fort Collins, "Pharmacology of Conditioning"

Senior High

Pamela Pratt, 12th grade, Wasson High School, Colorado Springs, "The Effects of Drugs on the Orb-Weaving Spiders"

Marine Technology Society

1st Place: Mark Dean, 8th grade, York Junior High School, Thornton, "Wave Machine (Motion, Construction, and Destruction)"

2nd Place: David Kyncl, 8th grade, Fort Morgan Junior High School, "Will Paraffin Contain Oil Spills in 1. Salt Water, 2. River Water, 3. Spring Water?"

Colorado Science Teachers Association

Junior High

Donald Ostwald, 8th grade, Fort Morgan Junior High School, Fort Morgan "Does Manure Work Better as a Fertilizer if Used in Combinations or if Used Alone?"

Senior High

Kevin Gertig, 12th grade, Rocky Ford High School, Rocky Ford, "Carbon Limitation in Algal Growth of Effluent as Predicted by Diurnal pH Patterns"

Aerospace and Electronics Systems Group of the Institute of Electrical and Electronics Engineers

Brian Pearsall, 11th grade, Montrose High School, Montrose, "A Low Cost Mini Computer Terminal"

Colorado Chapter of the Soil Conservation Society of America

Junior High

Donald Ostwald, 8th grade, Fort Morgan Junior High School, Fort Morgan "Does Manure Work Better as a Fertilizer if Used in Combinations or if Used Alone?"

Senior High

Oran Kanode, 11th grade, Highland High School, Ault, "The Micro World Below Your Feet"

Colorado Heart Association

1st Place: John Weist, 10th grade, Holyoke High School, Holyoke, "The Effect of Narcotics on the Heart Rate"

2nd Place: Andy Grant, 12th grade, Poudre High School, Fort Collins, "Genetic Influences Relating to Cholesterol Levels in Beagles"

Colorado Scientific Society

Junior High

Mark Dean, 8th grade, York Junior High School, Thornton, "Wave Machine (Motion, Construction, and Destruction)"

Molly Mills, 8th grade, Hill Junior High School, Denver, "A Simple Polarizing Microscope (15X) and Applications to Crystallography"

Colorado Mineral Society

Junior High

Danny Aldrich, 8th grade, Creede Junior-Senior High School, Creede, "An Experiment With Creede's Tailings Ponds"

Dennis Fulbright, 7th grade, Springfield Junior High School, Springfield, "Crystal Growing"

Senior High

Jack Heidrich, 11th grade, Brush High School, Brush, "The Kelvin Water-Drop Generator and the Relationship Between Dipole and Moments and Charge Build-up"

Kristina Johnson, 12th grade, Thomas Jefferson High School, Denver, "Holographic Study of the Spangiophore of Phycomyces"

Colorado Society of Clinical Pathologists and Colorado Society for Medical Technology

Junior High

1st Place: Mike Shima, 8th grade, Jefferson Junior High School, Rocky Ford, "A Comparison Study of Various Hand Cleansing Techniques"

2nd Place: Carolyn Wilson, 8th grade, Everitt Junior High School, Wheat Ridge, "What's So Bad About Cigarettes?"

Senior High

1st Place: Christine Specht, 12th grade, Poudre High School, Fort Collins, "A Rapid Microbial Technique for Determining the Age of Biological Specimens"

2nd Place: Craig Harper, 12th grade, Walsh High School, Walsh, "Surface Effects on Blood Coagulation"

Denver-Boulder Chapters of the Antennas and Propagation Society of the Institute of Electrical and Electronics Engineers

Mike Przekwas, 8th grade, St. Mary's of Littleton, "Demonstrating and Investigating the Laws of Reflection and Refraction"

Denver Section of the Institute of Electrical and Electronics Engineers

Junior High

Lisa Lynn Mallette, 8th grade, Broomfield Junior High School, Broomfield, "Let's Keep It Quiet!"

Senior High

Richard Tinkler, 11th grade, Montrose High School, Montrose, "Adapting a Digital Computer for Visual Capabilities"

Eastman Kodak Company

Richard Russel, 11th grade, St. Mary's High School, Colorado Springs, "Gamma Ray Induced Chromosomal Aberrations in Human Leukocytes"

Institute of Arctic and Alpine Research

Shawn Cass, 10th grade, McClave High School, McClave, "Cloud Seeding—Effect of Silver Iodide on Plants"

Mile High Chapter, Armed Forces Communication and Electronics Association

Richard Tinkler, 11th grade, Montrose High School, Montrose, "Adapting a Digital Computer for Visual Capabilities"

National Aeronautics and Space Administration

Junior High

Eric Mogren, 9th grade, Lincoln Junior High School, Fort Collins, "Effect of Dihdril of an Airfoil on the Lift of an Airfoil"

Senior High

Scot Heath, 12th grade, Frenchman RE-3, Fleming, "The Aerodynamics of a Frisbee"

National Park Service

Donald Beard, 10th grade, Hotchkiss High School, Hotchkiss, "Chiromids: Indicators Pollution"

Radio Shack

1st Place: Richard Tinkler, 11th grade, Montrose High School, Montrose, "Adapting a Digital Computer for Visual Capabilities"

2nd Place: Joseph Hughes, 12th grade, Wasson High School, Colorado Springs, "Order on a Non-Ordered Field"

3rd Place: Dorothy Bishop, 12th grade, Air Academy High School, Colorado Springs, "The Effects of Laser Rays on Agrobacterium Tumefaciens Cancer"

Rocky Mountain Association of Geologists

Junior High

1st Place: Mark Dean, 8th grade, York Junior High School, Thornton, "Wave Machine (Motion, Construction and Destruction"

2nd Place: David Kyncl, 8th grade, Fort Morgan Junior High School, Fort Morgan, "Will Paraffin Contain Oil Spills in 1. Salt Water, 2. River Water, 3. Spring Water?"

3rd Place: Monica Hobbs, 7th grade, Divine Redeemer, Colorado Springs, "The Road to Homo Sapiens"

Senior High

1st Place: Tom Corbridge, 12th grade, Cherry Creek High School, Englewood, "The Effects of the Soil pH on Watershed Erosion"

Rocky Mountain Bioengineering Society

1st Place: Glenn Hancock, 11th grade, Fairview High School, Boulder, "Robots"

2nd Place: Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, "Flying Insects"

Society for Technical Communication, Rocky Mountain Chapter

Junior High

1st Place—Written communications: Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, "Flying Insects"

1st Place—Graphics presentation: Michael McCarthy, 7th grade, Air Academy Junior High School, Colorado Springs, "The Fastest Mold Producing Substance"

Honorable Mention: Donald Ostwald, 8th grade, Fort Morgan Junior High School, Fort Morgan, "Does Manure Work Better as a Fertilizer if Used in Combinations or if Used Alone?"

Senior High

1st Place—Written communications: Robert Stamps, 10th grade, Wasson High School, Colorado Springs, "Power from Plasma"

1st Place—Graphics presentation: Ronald Nickell, 12th grade, Coronado High School, Colorado Springs, "The Effect of Methyl and Dimethyl Mercury on Rodents"

Honorable Mention: Carrie Kresl, 10th grade, Gateway High School, Aurora, "Entomology: To Control or Not to Control—That Is The Question"

Society of Women Engineers

Junior High
- 1st Place: Lisa Lynn Mallette, 8th grade, Broomfield Junior High School, Broomfield, "Let's Keep It Quiet!"
- 2nd Place: Kellie Peck, 8th grade, Olathe Junior High School, Olathe, "Fluidyne (Pump in a Bottle)
- Honorable Mention: Patty Sandborn, 8th grade, Lesher Junior High School, Fort Collins, Colorado, "Flying Insects"

Senior High
- 1st Place: Karen Tracy, 10th grade, Poudre High School, Fort Collins, "A Comparison of the Production of Methane and CO_2 from the Production of Animal and Plant Waste"
- 2nd Place: Diana Cox, 12th grade, Sangre de Cristo High School, Mosca, "The Little Stinker"
- 3rd Place: Glenda Biggs, 11th grade, Highland High School, Fort Collins, "The Influence of Testerone on Chick Embryos"

United States Air Force

Junior High
- Ruth Griswold, 9th grade, Lesher Junior High School, Fort Collins, "A Comparison of Radishes of Fungi on Response to Irradiation" (B)
- J. Austin Garrison, 8th grade, Lincoln Junior High School, Fort Collins, "Effect of Wrinkle Black Surface Treatment on Baseboard Convection" (E)
- Justin Marble, 9th grade, Arickaree School, Anton, "Endomorphisms of the Group Obtained by the Rotations of a Tetrahedron" (M)
- Peter Sandborn, 9th grade, Lesher Junior High School, Fort Collins, "Elasticity of Natural Fibers" (PS)
- Monica Hobbs, 7th grade, Divine Redeemer School, Colorado Springs, "The Road to Homo Sapiens" (Z))

Senior High
- Kent McLagan, 12th grade, Cherry Creek High School, Englewood, "Altitudinal Variation in Chlorophyll 'a' Structure in Englemann Spruce" (B)
- Paul Franchois, 11th grade, Rocky Mountain High School, Fort Collins, "Sound Adsorption Properties of Various Materials (E)
- Joseph Hughes, 12th grade, Wasson High School, Colorado Springs, "Order on a Non-Ordered Field" (M)
- Scot Heath, 12th grade, Frenchman RE-3, Fleming, "The Aerodynamics of a Frisbee" (PS)
- Richard Russel, 11th grade, St. Mary's High School, Colorado Springs, "Gamma Ray Induced Chromosomal Aberrations in Human Leukocytes" (Z)

United States Army

Junior High
- Danny Aldrich, 8th grade, Creede Junior High School, Creede, "An Experiment with Creede's Tailings Pond" (PS)
- Valerie Boughman, 9th grade, Yuma High School, Yuma, "Sound vs Retention, Part III" (Z)
- Mark Dean, 8th grade, York Junior High School, Thornton, "Wave Machine (Motion, Construction, and Destruction)" (E)
- J. Austin Garrison, 8th grade, Lincoln Junior High School, Fort Collins, "Effect of Wrinkle Black Surface on Baseboard Convection" (E)
- David Kyncl, 8th grade, Fort Morgan Junior High School, Fort Morgan, "Will Paraffin Contain Oil Spills in 1. Salt Water, 2. River Water, 3. Spring Water?" (PS)

Senior High
- Rex Craig, 10th grade, Prairie High School, New Raymer, "The Zinc-Ion Laser: Composite Fringe Signal Analysis" (PS) Bronze Medallion
- Dorothy Bishop, 12th grade, Air Academy High School, Colorado Springs, "The Effects of Laser Rays on Agrobacterium Tumefaciens Cancer" (B)
- Glen Hancock, 11th grade, Fairview High School, Boulder, "Robots" (E)
- Craig Harper, 12th grade, Walsh High School, Walsh, "Surface Effects on Blood Coagulation" (Z)
- Jack Heidrich, 11th grade, Brush High School, Brush, "The Qualitative and Quantitative Analysis of Underground Streams in Morgan County" (E)
- Eric Olsen, 12th grade, Brush High School, Brush, "The Kelvin Water-Drop Generator and the Relationship Between Dipole Moments and Charge Build-up" (E)
- Robert Stamps, 10th grade, Wasson High School, Colorado Springs, "Power from Plasma" (PS)

U.S. Department of Commerce

Dave Lovering, 12th grade, Lakewood High School, Lakewood, "Space-Time Curvature and the Propagation of Gravitational Radiation"

United States Navy

- 1st Place: Kristina Johnson, 12th grade, Thomas Jefferson High School, Denver, Holographic Study of the Sporangiophore of Phycomyces"
- 2nd Place: Mike Mayberry, 12th grade, Fort Morgan High School, Fort Morgan, "Distribution of the Prime Twins"

John Wiley & Sons, Writing Award

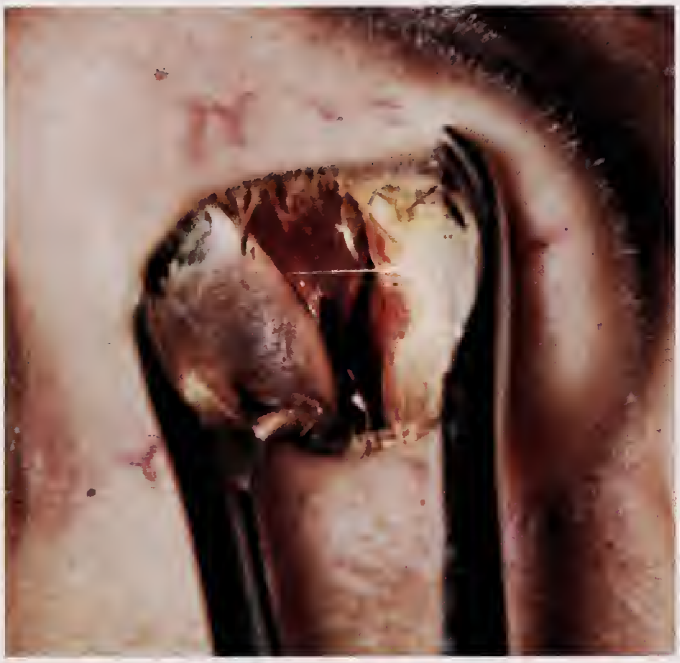
Jeffrey Gonzales, 10th grade, St. Mary's, Colorado Springs, "Psychogaloanic Responses of the Mimosa Pudica, Philodendron Cordatum and Sansevieria Trifasciata Under Various Stimuli"

Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

But right now, whether he's got allergic rhinitis or a cold, he's suffering from the same irritating symptoms of drip, congestion and stuffiness. Try DIMETAPP EXTENTABS®. They're formulated to relieve these symptoms without much chance of causing drowsiness or overstimulation. Your patients will appreciate the 24-hour relief they can get from just one tablet every 12 hours.

Cold or Allergy?



Whether it's a cold or an allergy, Dimetapp Extentabs® effectively relieve stuffiness, drip and congestion.

INDICATIONS: Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses, such as the common cold, seasonal allergies, sinusitis, rhinitis, conjunctivitis and otitis. In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions, thereby affording relief from nasal stuffiness and postnasal drip.

CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class. Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age. Because of its drying and thickening effect on the lower respiratory secretions Dimetapp is not recommended in the treatment of bronchial asthma Also, Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy.

WARNINGS: *Use in children:* In infants and children particularly, antihistamines in overdosage may produce convulsions and death.

PRECAUTIONS: Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery, etc. Patients receiving antihistamines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics, sedatives, tranquilizers, etc.

ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash urticaria, leukopenia, agranulocytosis, and thrombocytopenia; drowsiness, lassitude, giddiness, dryness of the mucous membranes, tightness of the chest thickening of bronchial secretions, urinary frequency and dysuria, palpitation, hypotension/hypertension, headache, faintness, dizziness, tinnitus, incoordination, visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect, anorexia, nausea, vomiting, diarrhea, constipation, and epigastric distress

HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg.

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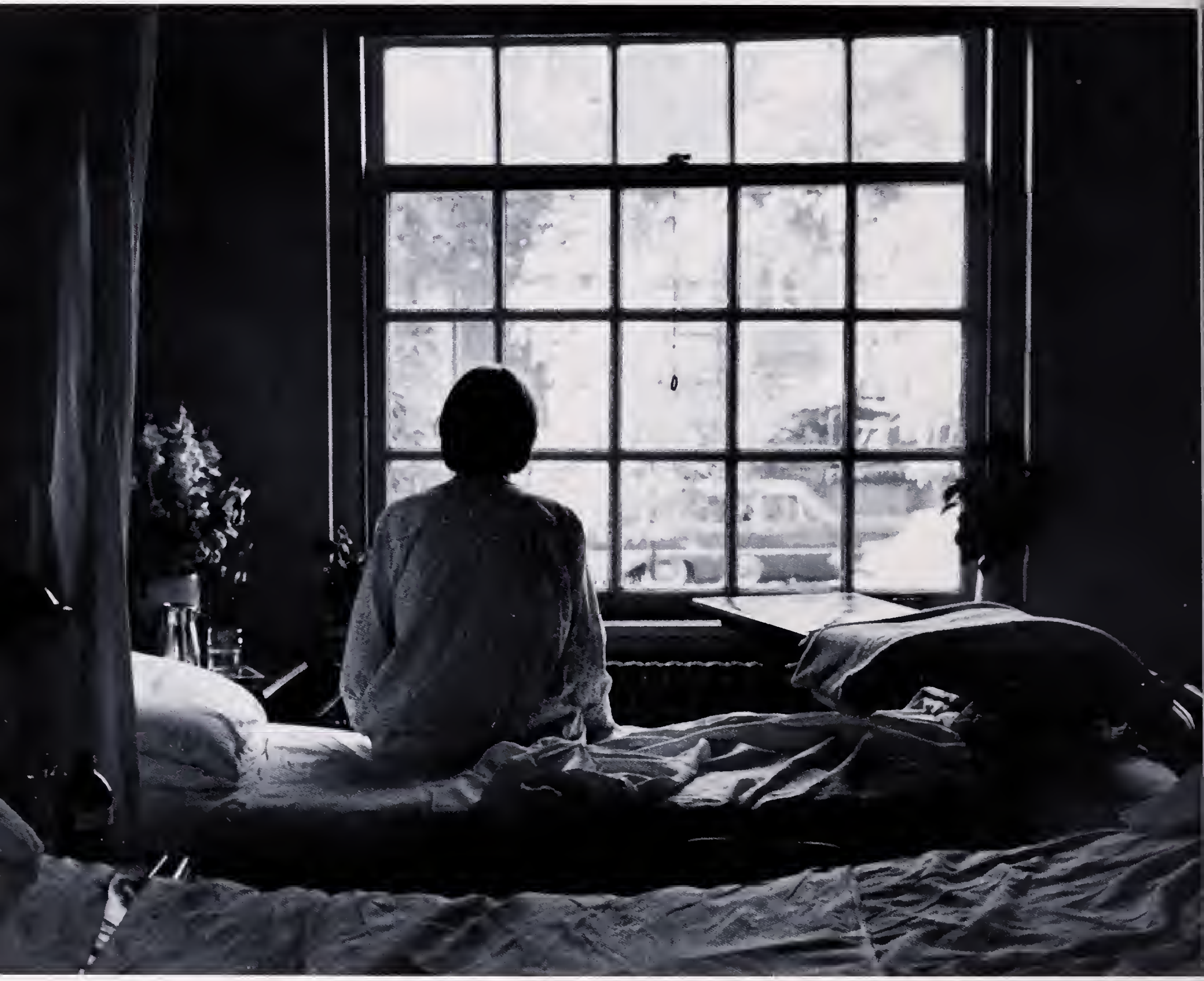
A. H. Robins Company, Richmond, Va. 23220

when pain goes on... and on... and on–



For the patient with a terminal illness, PAIN past, present, and future can dominate his thoughts until it becomes almost an obsession. The more he is aware of the pain he is now experiencing, the more difficult it is to erase his memory of yesterday's pain, and to allay his fearful anticipation of tomorrow's pain.

Surely the last thing this patient needs is an analgesic containing caffeine to stimulate the senses and heighten pain awareness. A far more logical choice is Phenaphen with Codeine. The sensible formula provides ¼ grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can help control the pain more effectively. Don't you agree, Doctor, that psychic distress is an important factor in most of your terminal and long-term convalescent patients?

the analgesic formula that calms instead of caffeinates

Phenaphen® with Codeine

Phenaphen with Codeine No. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Codeine phosphate, ¼ gr. (No. 2), ½ gr. (No. 3) or 1 gr. (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature

CIII Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

A. H. Robins Company, Richmond, Va. A·H·ROBINS

MEETINGS

American Geriatrics Society

A DAY IN GERIATRIC THERAPEUTICS

Stouffer's Denver Inn, 3203 Quebec, Denver, Colorado

June 17, 1975

Contact: Frank McGlone, MD, 701 East Colfax Ave., Denver, Colorado 80203

Credit: 6 hours AAFP

University of Colorado Medical Center

PATHOLOGY IN GYNECOLOGY AND OBSTETRICS

Given Institute of Pathobiology Aspen, Colorado

June 30 - July 4, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

Colorado Academy of Family Physicians

ANNUAL MEETING

Manor Vail, Vail, Colorado

July 11-13, 1975

Contact: Mrs. Shirlee Myers, 1601 East 19th Avenue, Denver, Colorado 80218

American Academy of Family Physicians

18TH ANNUAL RUIDOSO SUMMER CLINIC

Ruidoso, New Mexico

July 14-17, 1975

Contact: Bob Reid, P.O. Box 456, Sunland Park, New Mexico 88063

American Psychiatric Association-American Psychological Association

PERSONAL VALUES IN PROFESSIONAL PRACTICE

The Stonebridge Inn, Snowmass-at-Aspen, Colorado

July 20-25, 1975

Contact: American Psychiatric Association, 1700 18th Street, NW, Washington, D.C. 20009

American Society for Surgery of the Hand

INTERNATIONAL SYMPOSIUM OF HAND SURGERY

The Lodge, Vail, Colorado

July 21-25, 1975

Contact: John A. Boswick, Jr., MD, 4200 East 9th Ave., Denver, Colorado, Container #2414, 80220.

Colorado Psychiatric Society

MIDSUMMER MEETING

Snowmass-at-Aspen, Colorado

July 25-27, 1975

Contact: Shirlee Myers, 1601 East 19th Avenue, Denver, Colorado 80218.

University of Colorado School of Medicine, Continuing Medical Education

PEDIATRICS

Given Institute of Pathobiology, Aspen, Colorado

July 27-30, 1975

* * *

DERMATOLOGY

Given Institute of Pathobiology, Aspen, Colorado

July 31-August 2, 1975

* * *

CLINICAL GASTROENTEROLOGY: CURRENT TOPICS AND CONTROVERSIES

The Gant, Aspen, Colorado

August 4-8, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

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Exciting family vacation in high mountain valley. Your own log cabin with bath, excellent ranch-style meals; top-notch horses. Trout stream through ranch. Write: Dewey Dominick, MD, Box 109, Cody, Wyoming 82414; or phone (307) 587-3185 or 587-3997.

29th Annual

Rocky Mountain Cancer Conference

Brown Palace Hotel, Denver, Colorado

July 18-19, 1975

Co-sponsored by the American Cancer Society, Colorado Division
and the Colorado Medical Society

NO REGISTRATION FEE

Approved for AAFP Credit

A fine scientific meeting with an outstanding panel of renowned physicians

Friday, July 1

Morning Session Ballroom "A"

8:00 a.m. — REGISTRATION—Promenade
(Coffee served)

8:30 a.m. — FILM—"Acute Leukemia Report, 1974"

9:00- 9:15 a.m. — WELCOME

Edward E. Tennant, MD
President, Colorado Division,
American Cancer Society

George P. Rosemond, MD
President,
American Cancer Society

Howard T. Robertson, MD
President,
Colorado Medical Society

Malcolm C. Todd, MD
President,
American Medical Association

9:15- 9:45 a.m. — **Evaluation and Management of Anorexia in Cancer Patients**
William D. DeWys, MD
Associate Professor of Medicine
Medical Oncology Section
Northwestern University
Chicago, Illinois

9:45-10:15 a.m. — **External Signs of Internal Malignancies**
Henry M. Lewis, MD
Dermatologist, Private Practice
Denver, Colorado

10:15-10:30 a.m. — COFFEE BREAK—Promenade

10:30-11:00 a.m. — **Cancer In Immunosuppressed Patients**
Israel Penn, MD
Associate Professor of Surgery
University of Colorado School of Medicine, Denver, Colorado

11:00-11:30 a.m. — **Disorders of Hemapoiesis Associated With Non-Hematologic Malignancies**
George H. Curfman, Jr., MD
Internal Medicine, Private Practice, Denver, Colorado

12:00 Noon — LUNCHEON
Future of the AMA
Malcolm C. Todd, MD

Afternoon Session

1:45- 2:15 p.m. — **Cushing's Syndrome**
Mortimer B. Lipsett, MD
Professor of Medicine
Case Western Reserve University
Director, The Cancer Center, Inc.
Cleveland, Ohio

2:15- 2:45 p.m. — **Cancer: Remote Effects on the Nervous System**
Michael Cherington, MD
Assistant Clinical Professor of Neurology, University of Colorado School of Medicine

2:45- 3:00 p.m. — COKE/COFFEE BREAK—Promenade

3:00- 3:30 p.m. — **Malignant Pain; Its Management**
William T. Warmath, MD
Neurological Surgeon, Private Practice, Denver, Colorado

3:30- 5:00 p.m. — PANEL DISCUSSION:
Surgical Aspects of Paraneoplastic Syndromes
Moderator:
Ben Eiseman, MD
Director, Department of Surgery
Denver General Hospital
Denver, Colorado

Panel Members:
Stephen Engel, MD
General Surgeon, Private Practice, Denver, Colorado

George E. Moore, MD
Director, Department of Surgical Research, Denver General Hospital, Denver, Colorado

William R. Nelson, MD
Tumor Surgeon, Private Practice, Denver, Colorado
George P. Rosemond, MD

Saturday, July 19

8:00 a.m. — REGISTRATION—Promenade
(Coffee Served)

8:30- 9:00 a.m. — FILM—"Detecting Breast Cancer Earlier"

9:00- 9:30 a.m. — **Breast Cancer Today**
George P. Rosemond, MD

9:30-10:00 a.m. — **Gonadtropins and Cancer**
Mortimer B. Lipsett, MD

10:00-10:30 a.m. — **Pathogenesis of Cancer Cachexia**
William D. DeWys, MD

10:30-10:45 a.m. — COFFEE BREAK

10:45-11:15 a.m. — **Renal Manifestations of Neoplastic Disease**
Wagner J. Schorr, MD
Nephrologist, Private Practice, Denver, Colorado

Cancer Committee Chairman:
Edward E. Tennant, MD
Sterling, Colorado
President, Colorado Division, ACS

Conference Program Chairman:
Joseph L. Kovarik, MD
Denver, Colorado
Member, Executive Committee of the Colorado Division, ACS

For complete program call or write

American Cancer Society, Colorado Division, Inc.
1809 East 18th Avenue, Denver, Colorado 80218
Phone: 321-2464

OBITUARIES

Vinton A. Muller, MD, Reno, died February 21, 1975 in Reno at the age of 82. He had practiced surgery over 41 years, and had retired in 1962.

He was born in Nevada City, California, December 3, 1892 to Dr. and Mrs. Carl L. Muller. His father practiced medicine in that city up to his death in 1918. Dr. Muller attended the University of California at Berkeley, and had resident surgical training in San Francisco at the UC Medical School. He then moved to Reno.

He served as consultant to various hospitals and business companies, was past president, secretary and a member of the Washoe County Medical Society, as well as a past president and member of the Nevada State Medical Association. He was a member of the American Medical Association and a Fellow of the American College of Surgeons.

He helped establish the first blood plasma bank in Reno, and was a founder of the Reno Surgical Society. He served for eight years as chief medical adviser to the Nevada Industrial Commission during the period in which the Hoover Dam was under construction.

He was a member of the Reno Lodge No. 13 F & AM, BPO Elks Lodge, No. 597, the Washoe County Sheriff's Aero Squadron, and the Quiet Birdmen Aviation Society.

In 1922 he was married to Maizie Ruth Kinder who died in 1970. A nephew, William Kinder, Roxborough, Pennsylvania, survives.

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*This drug has been evaluated as "probably" effective for this indication.

See brief summary of prescribing information on facing page for Indications, Contraindications, Warnings, Precautions and Adverse Reactions.

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a nonsalicylate analgesic equal to aspirin for relief of pain,[1,2] yet unlikely to cause the gastric irritation,[2,3] allergic reactions[2] or increased bleeding time[4] associated with aspirin therapy...

and a skeletal muscle relaxant shown in extensive clinical studies to afford relief of discomfort in acute musculoskeletal conditions*[5-7] but which is not an antihistamine or tranquilizer derivative and is unlikely to produce a tranquilizing or sedative effect.[5,7,8]

***Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

"Probably" effective as an adjunct to rest and physical therapy for the relief of discomfort associated with acute, painful musculoskeletal conditions. The mode of action of this drug has not been clearly identified, but may be related to its sedative properties. Chlorzoxazone does not directly relax tense skeletal muscles in man.

Contraindications: Sensitivity to either component.
Warnings: *Usage in Pregnancy*—Use in women of childbearing potential only when potential benefits outweigh possible risks.
Precautions: Exercise caution in patients with known allergies or history of drug allergies. If a sensitivity reaction or any signs or symptoms suggestive of liver dysfunction are observed, the drug should be stopped.
Adverse Reactions: Occasionally, drowsiness, dizziness, lightheadedness, malaise, overstimulation or gastrointestinal disturbances may be noted; rarely, allergic-type skin rashes, petechiae, ecchymoses, angioneurotic edema or anaphylactic reactions. In rare instances, chlorzoxazone may possibly have been associated with gastrointestinal bleeding. While PARAFLEX® (chlorzoxazone) tablets and other chlorzoxazone-containing products have been suspected as being the cause of hepatic toxicity in approximately twenty-four patients, it was not possible to state that the dysfunction was or was not drug induced.
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References: 1. Batterman, R.C., and Grossman, A.J.: Fed. Proc. *14*:316, 1955. **2.** Goodman, L.S., and Gilman, A., ed.: The Pharmacological Basis of Therapeutics, ed. 4. New York, The Macmillan Company, 1970. **3.** Vickers, F.N.: Gastroint. Endosc. *14*:94, 1967. **4.** Mielke, C.H., Jr., and Britten, A.F.H.: New Engl. J. Med. *282*:1270, 1970 (Corresp.). **5.** Vernon, W.G.: Curr. Therap. Res. *14*:801, 1972. **6.** Scheiner, J.J.: Curr. Therap. Res. *14*:168, 1972. **7.** Walker, J.M.: Curr. Therap. Res. *15*:248, 1973. **8.** Data on file, McNeil Laboratories, Inc.

†U.S. Patent No. 2,895,877

McNEIL McNeil Laboratories, Inc.
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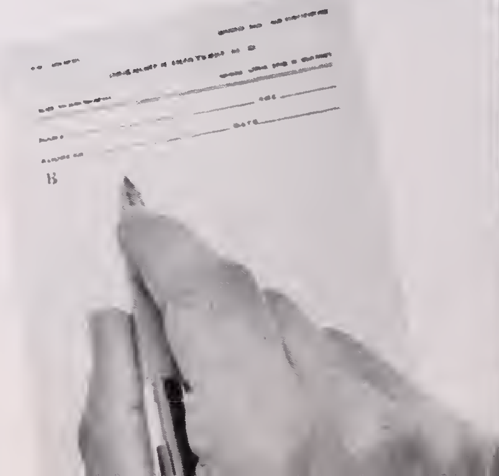
Bioequivalence



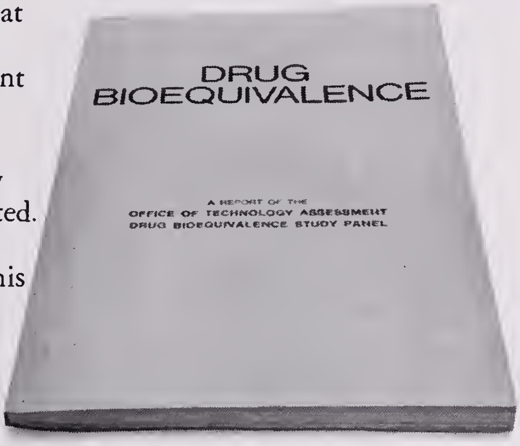
he weight of scientific opinion:

If the pharmacist substituted a emically equivalent drug for the e you have specified for your atient—could you be certain of that roduct's safety and effectiveness mply because the chemical content as the same?

Definitely not, unless bio-quivalence tests and other quality ssurance checks had been conducted. he pharmaceutical industry and any scientists have maintained this osition for years, but others have uestioned it. Now the Office of echnology Assessment of the ongress of the United States has eported on the issue in its Drug ioequivalence Study.*

Here are a few definitive state-nents in the O.T.A. report:

"...the problem of bioinequiva-ency in chemically equivalent prod-cts is a real one. Since the studies in which lack of bioequivalence was lemonstrated involved marketed roducts that met current compen-ial standards, these documented in-tances constitute unequivocal vidence that neither the present tandards for testing the finished roduct nor the specifications for materials, manufacturing process, and controls are adequate to ensure that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.


DRUG
BIOEQUIVALENCE
A REPORT OF THE
OFFICE OF TECHNOLOGY ASSESSMENT
DRUG BIOEQUIVALENCE STUDY PANEL

"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

The Pharmaceutical Manufacturers Association supports federal legislative amendments that would require manufacturers of duplicate prescription pharmaceutical products, subject to new drug procedures, to document:

(a) chemical equivalence; and
(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or
(c) where such validation is not possible, therapeutic equivalence.

In addition, the PMA supports federal legislation that would require certification of all manufacturers of prescription products before they could start in business, annual inspections and certification thereafter, and strict adherence to FDA regulations on good manufacturing practices.

The overall quality of the United States drug supply is excellent. But only a total quality assurance program, envisaged in these and other policy positions adopted by the PMA Board of Directors in 1974, can bring about acceptable levels of performance by all prescription drug manufacturers and thereby assure the integrity of your prescription...

P·M·A

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*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

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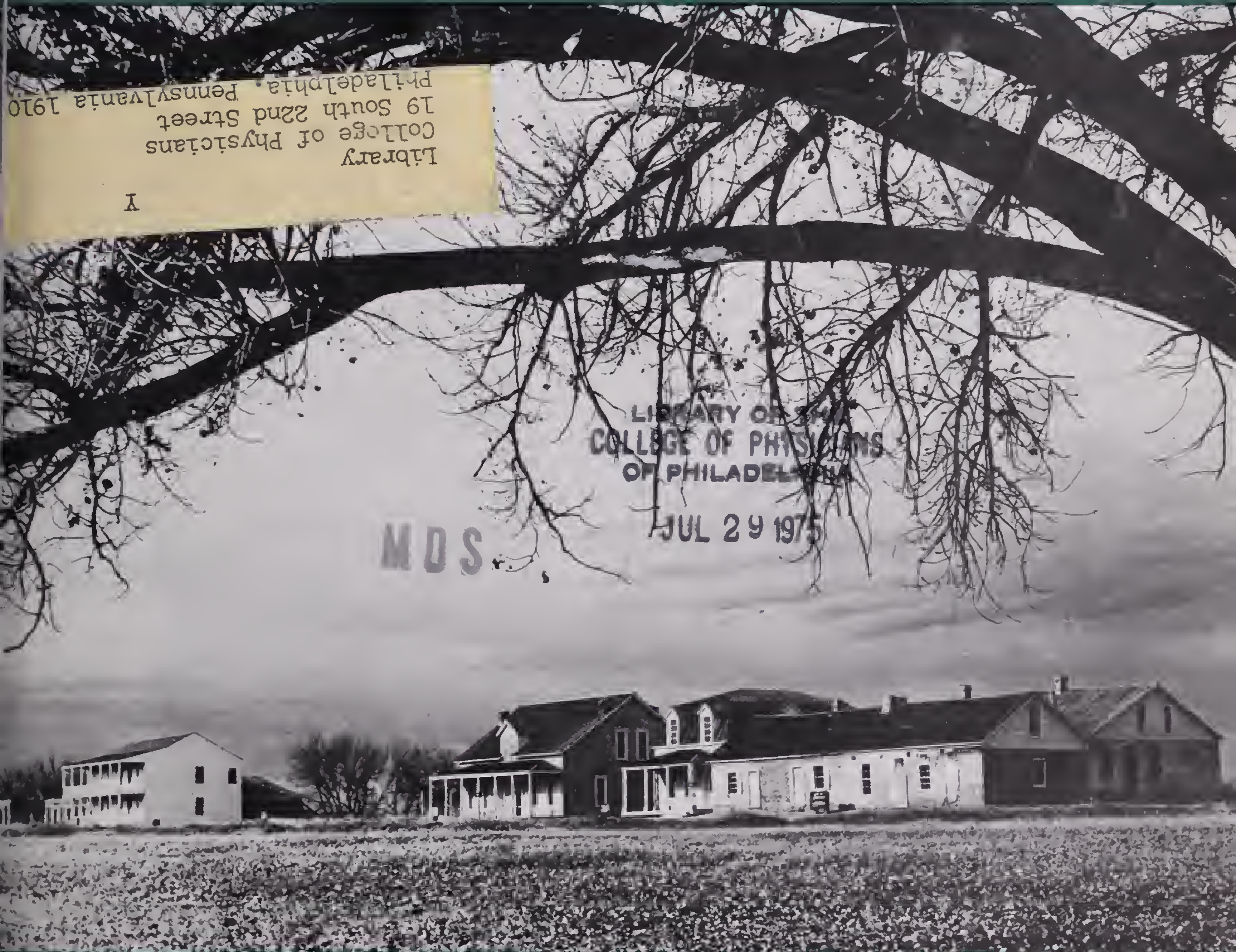

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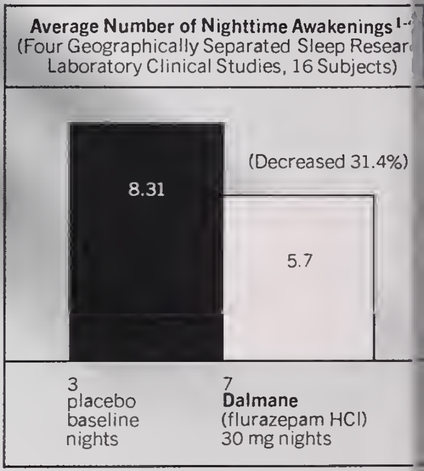

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…and is well tolerated. The sual adult dosage is 30 mg *h.s.*, ut with elderly and debilitated atients, limit the initial dose to 5 mg to preclude oversedation, izziness or ataxia. Evaluation of ossible risks is advised before rescribing.

EFERENCES:

Karacan I, Williams RL, Smith JR: The eep laboratory in the investigation of sleep nd sleep disturbances. Scientific exhibit at e 124th annual meeting of the American sychiatric Association, Washington DC, ay 3-7, 1971

Frost JD Jr: A system for automatically nalyzing sleep. Scientific exhibit at the 4th annual Clinical Convention of the merican Medical Association, Boston, ov 29-Dec 2, 1970; and at the 42nd annual cientific meeting of the Aerospace Medical ssociation, Houston, Apr 26-29, 1971

. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

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efore prescribing Dalmane (flurazepam Cl), please consult complete product nformation, a summary of which follows:

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ontraindications: Known hypersensitivity o flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

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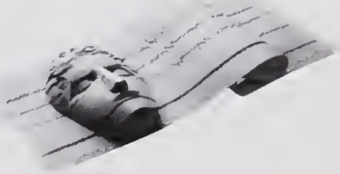

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Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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*Higgs, R. H., Smyth, R. D., and Castell, D. O., Gastric Alkalinization—Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin, *The New Engl. J. of Med.*, 291, 486-490, 1974.

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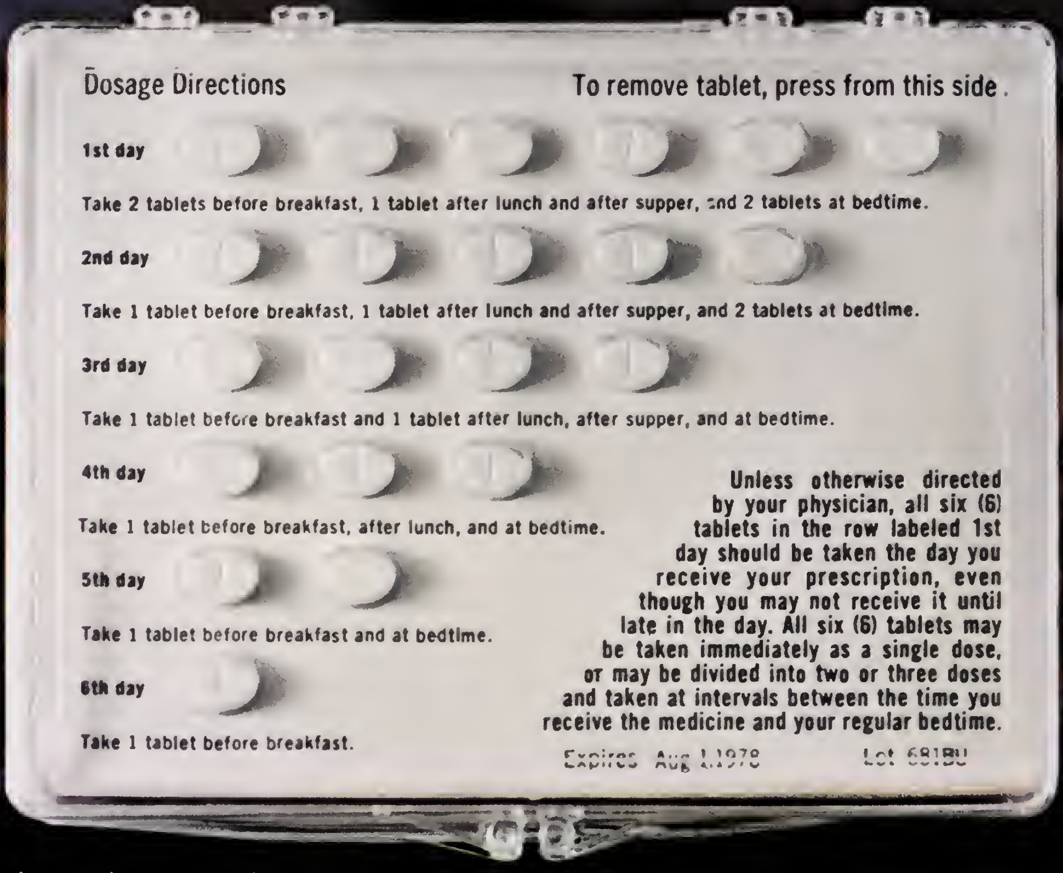

Dosage Directions

To remove tablet, press from this side.

1st day

Take 2 tablets before breakfast, 1 tablet after lunch and after supper, and 2 tablets at bedtime.

2nd day

Take 1 tablet before breakfast, 1 tablet after lunch and after supper, and 2 tablets at bedtime.

3rd day

Take 1 tablet before breakfast and 1 tablet after lunch, after supper, and at bedtime.

4th day

Take 1 tablet before breakfast, after lunch, and at bedtime.

5th day

Take 1 tablet before breakfast and at bedtime.

6th day

Take 1 tablet before breakfast.

Unless otherwise directed by your physician, all six (6) tablets in the row labeled 1st day should be taken the day you receive your prescription, even though you may not receive it until late in the day. All six (6) tablets may be taken immediately as a single dose, or may be divided into two or three doses and taken at intervals between the time you receive the medicine and your regular bedtime.

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The explicit printed dosage instructions that accompany each Dosepak make it easy for the patient to understand and follow the dosage regimen.

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tractable to adequate trials of conventional
eatment will often respond to a short,
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edrol Dosepak is designed to provide a tapered,
x-day course of methylprednisolone tablets.

n occasion, a six-day course of Medrol therapy
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be extended. If there is continued contact
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ill not completely suppress the inflammatory
sponse. A further caution: If lesions become
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sistance to infection and hinder the body's
bility to localize an infection.

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SCRIPTION AND ACTIONS: Medrol (methylprednisolone) is a synthetic glucocor-
id with potent anti-inflammatory effects. It is readily absorbed from the GI tract.
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ne responses to diverse stimuli.
DICATIONS: 1. **Endocrine Disorders:** Primary or secondary adrenocortical insuf-
iency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used
conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid
pplementation is of particular importance). Congenital adrenal hyperplasia; nonsup-
rative thyroiditis; hypercalcemia associated with cancer. 2. **Rheumatic Disorders:** As
junctive therapy for short-term administration (to tide the patient over an acute epi-
de or exacerbation) in: psoriatic arthritis; rheumatoid arthritis (selected cases may
quire low-dose maintenance therapy); ankylosing spondylitis; acute and subacute
rsitis; acute nonspecific tenosynovitis; acute gouty arthritis. 3. **Collagen Diseases:**
uring an exacerbation or as maintenance therapy in selected cases of—Systemic
pus erythematosus; acute rheumatic carditis. 4. **Dermatologic Diseases:**
mphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-
hnson syndrome); exfoliative dermatitis; mycosis fungoides; severe psoriasis. 5.
llergic States: Control of severe or incapacitating allergic conditions intractable to
equate trials of conventional treatment: Seasonal or perennial allergic rhinitis; bron-
ial asthma; contact dermatitis; atopic dermatitis; serum sickness. 6. **Ophthalmic**
iseases: Severe acute and chronic allergic and inflammatory processes involving the
e and its adnexa such as—allergic corneal marginal ulcers; herpes zoster ophthal-
icus; anterior segment inflammation; diffuse posterior uveitis and choroiditis; sympa-
etic ophthalmia; allergic conjunctivitis; keratitis; chorioretinitis; optic neuritis; iritis
d iridocyclitis. 7. **Respiratory Diseases:** Symptomatic sarcoidosis; Loeffler's syn-
ome not manageable by other means; berylliosis; fulminating or disseminated pulmo-
ary tuberculosis when concurrently accompanied by appropriate antituberculous
emotherapy. 8. **Hematologic Disorders:** Idiopathic and secondary thrombocytopenia
adults; acquired (autoimmune) hemolytic anemia; erythroblastopenia (RBC anemia);
ongenital (erythroid) hyperplastic anemia. 9. **Neoplastic Diseases:** For palliative man-
gement of: leukemias and lymphomas in adults; acute leukemia of childhood. 10.
dematous States: To induce a diuresis or remission of proteinuria in the nephrotic
yndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.
1. **Miscellaneous:** Tuberculous meningitis with subarachnoid block or impending
lock when concurrently accompanied by appropriate antituberculous chemotherapy.
ystemic dermatomyositis (polymyositis).
ONTRAINDICATIONS: Systemic fungal infections.
ARNINGS: In patients on corticosteroid therapy subjected to unusual stress, in-
reased dosage of rapidly acting corticosteroids before, during, and after the stressful
ituation is indicated.
Corticosteroids may mask some signs of infection and new infections may appear
uring their use. There may also be decreased resistance and inability to localize infec-
on. Prolonged use may enhance the establishment of secondary ocular infections due
o fungi or viruses.
Since adequate human reproductive studies have not been done, the use in preg-
ancy, nursing mothers or women of childbearing potential requires that the possible
enefits be weighed against the potential hazards to the mother and the embryo or
etus. Infants should be observed for signs of hypoadrenalism.
Average and large doses of hydrocortisone or cortisone can cause elevation of blood
ressure, salt and water retention, and increased excretion of potassium. These effects
re less likely to occur with the synthetic derivatives except when used in large doses.
Dietary salt restriction and potassium supplementation may be necessary. All corticos-
eroids increase calcium excretion.
While on corticosteroid therapy, patients should not be vaccinated against small-
ox. Other immunization procedures should not be undertaken in patients who are
on corticosteroids, especially on high dose, because of possible hazards of neuro-
logical complications and a lack of antibody response.
The use of corticosteroids in active tuberculosis should be restricted to those cases
of fulminating or disseminated tuberculosis in which the corticosteroid is used for the
management of the disease in conjunction with an appropriate antituberculous regi-
men.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

PRECAUTIONS: Hormone therapy is an adjunct to, and not a replacement for, conventional therapy.

Dosage should be individualized according to the severity of the disease and the response of the patient. As soon as a satisfactory clinical response is obtained, the daily dose should be reduced, either to termination of treatment or to the minimal effective maintenance dose level. The lowest possible dose should be used and when reduction in dosage is possible, the reduction should be gradual if the drug has been administered for more than a few days. If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Drug-induced secondary adrenocortical insufficiency may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Psychic derangements may appear or existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia..

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Blood pressure, body weight, routine laboratory studies, including 2-hour postprandial blood glucose and serum potassium, and a chest X-ray should be obtained at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with known or suspected peptic ulcer disease.

ADVERSE REACTIONS: Fluid and Electrolyte Disturbances. Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension. **Musculoskeletal.** Muscle weakness; steroid myopathy; loss of muscle mass; osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones. **Gastrointestinal.** Peptic ulcer with possible perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis. **Dermatologic.** Impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating. May suppress reactions to skin tests. **Neurological.** Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment. Convulsions; vertigo; headache. **Endocrine.** Development of Cushingoid state; suppression of growth in children; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; menstrual irregularities; decreased carbohydrate tolerance; manifestations of latent diabetes mellitus; increased requirements for insulin or oral hypoglycemic agents in diabetics. **Ophthalmic.** Posterior subcapsular cataracts; increased intraocular pressure; glaucoma; exophthalmos. **Metabolic.** Negative nitrogen balance due to protein catabolism.

DOSAGE AND ADMINISTRATION: The initial dosage may vary from 4 to 48 mg per day. **Requirements are variable and must be individualized on the basis of the disease under treatment and the response of the patient.** The proper maintenance dosage should be determined by decreasing the initial dosage in small decrements at appropriate time intervals until the lowest dosage which will maintain an adequate clinical response is reached. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

ALTERNATE-DAY THERAPY (ADT): ADT is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects including pituitary-adrenal suppression, the Cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.

Medrol (methylprednisolone) or other short-acting (producing adrenocortical suppression for 1¼ to 1½ days following a single dose) corticoids are recommended for ADT. Complete control of symptoms will not be possible in all patients. When considering this mode of therapy, keep in mind the basic principles and indications for corticosteroid therapy. The benefits of ADT should not encourage the indiscriminate use of steroids.

SUPPLIED: 2 mg—in bottles of 30 and 100 scored tablets; **4 mg**—in bottles of 30, 100 and 500 scored tablets and in 21 scored tablet Dosepak™ ; **16 mg**—in bottles of 50 scored tablets and in 14 scored tablet ADT Pak® (formerly Alternate Daypak®).

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For acute cystitis*

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Basic therapy with convenience:

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*Nonobstructed; due to susceptible strains of *E. coli*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. ***Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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"United We Stand . . . ."

"WE MUST ALL HANG TOGETHER, or assuredly we shall hang separately."—Benjamin Franklin.

Thus has been stated what impresses me as an important problem facing the medical profession today. Physicians are, by their very nature, highly individualistic persons. Each of us is accustomed to making decisions all day, every day, each one of them reached as an individual and necessarily reached by the deliberate resistance to outside forces or pressures which we feel should not influence that decision.

Having deliberately trained ourselves to be independent, it is the simplest thing in the world for each of us to ignore what our colleagues have to say. It is equally easy for us to say we will act according to the dictates of our own individualistic thinking, having no regard for the need to adjust our personal convictions so that they can coincide with all or nearly all other physicians.

We live in a time when the profession must every day deal with outside forces of great magnitude. These forces, such as governments, insurance companies, the lay public, and the press, exert a unified pressure against us.

We, who represent physicians as officers of societies, cannot serve effectively as your advocates nor represent you at the negotiating table unless we have your willingness to support those actions, and your active involvement in the development of positions to be taken.

Each physician must learn to weigh his own personal likes and dislikes against the needs of the profession itself and to make adjustments in his own responses so that our position will be one of strength supported by common convictions. Support your medical organizations and be active in them.

Signed

Donald B. Hunton, MD
President, Wyoming State Medical Society
Cheyenne

Expressed in another way

INDEPENDENCE OF ACTION OF the individual physician has long been a bedrock principle of organized medicine. However, the events of history and the increasing complexity of the society in which we find ourselves are forcing an unwelcome reevaluation of this precept. In the ever-increasing circles of regulation, third-party insurors, responsibilities, professional liability demands, consumer groups and sophistication of the health care delivery system which surrounds the medical practitioner, there is one continuous feature which jumps out at an objective viewer's eye—only the physician still operates as an individual, or as a group of individuals.

This numbing fact places the medical practitioner at a disadvantage from which many times he never recovers in his negotiations with government, large third-party insurors, or in seeking to tell his story in competition with the Ralph Naders or those who would destroy the health care system in America today to build their version of a utopia of medical care.

To reduce the odds in this perpetual battle, the individual physician has turned to his fellows and formed professional societies at the county, state, specialty, and national level. But, he has reserved the right to step aside from the group if they did not support every element of his philosophy and his every idea. In short, he has said, "The Society (or Association) speaks for medicine, but I will not be bound by my peers' decision." It is probably a sad commentary on our world, but this freedom of the individual is rapidly dwindling. The physician is coming face-to-stone wall if he seeks to singly confront the many organized groups concerned with health care.

State and local physician groups must take the leadership in their spheres to draw a consensus from their members, and speak forcibly and forthrightly in representing their members. The individual doctor must give his ideas and input freely and then stand behind the decisions of his peers as they negotiate in his behalf. Only when physicians stand together, as many in this country are beginning to do in the professional liability crisis, will physicians gain the leverage to talk on equal terms with those who would change the profession beyond recognition.

> "A wise man adapts himself to circumstances as water adapts itself to the vessel that contains it." —Chinese Proverb.

But the water is not changed.

Robert G. Smith
Executive Secretary
Wyoming State Medical Society
Cheyenne

Gastroscopy in Surgical Practice

Over the past two years the new fiberoptic gastroscope has literally "opened" by eyes. I have used the rigid tube for endoscopy for many years and, in addition, the old side-viewing gastroscope, but I was not ready for the experience of this new instrument! The first table illustrates the types of pathology encountered in 100 gastroscopies and their relative frequency. These categories are arbitrary divisions and represent the clinical problems posed by the groups of patients studied.

The gastroscope has not contributed significantly to the diagnosis or evaluation of hiatus hernia because the rigid scope is easy to pass and affords good visualization of the entire esophagus. However, one extremely significant contribution of the new instrument is the ability to go beyond the level of the hernia and reflux esophagitis to examine the stomach and duodenum, searching for frequently found coexisting pathology. The finding of a gastric or duodenal ulcer in cases in which the pathology was not suspected by x-ray is a definite plus.

TABLE 1

CATEGORIES OF CLINICAL STATES IN ONE HUNDRED CASES

Hiatal Hernia	22
Esophageal Cancer	3
X-ray normal but ulcer found	12
Post-gastrectomy pathology	15
X-ray abnormal and confirmed	28
X-ray normal and confirmed	20

The diagnosis and management of carcinoma of the esophagus has also not been drastically altered by the fiberoptic instruments except for the ability to evaluate the stomach distal to the tumor. Certainly, the small biopsy specimens through the fiberoptic scope are not nearly as adequate as the large bites that can be obtained through the large metal scopes.

The category entitled "X-ray normal, but gastric or duodenal ulcer found" is undoubtedly the most important new advantage in gastroscopy. This advance is illustrated by the demonstration of a penetrating posterior duodenal ulcer in a middle-aged man who had been extremely symptomatic over a period of many years and had repeated negative radiographic examinations of his upper-gastrointestinal tract. But how do you decide to gastroscope in the event that the x-ray is read as normal, realizing that the radiologists are accurate in the vast majority of instances? It is our opinion that if a patient has prominent and persistent symptoms in the face of a negative x-ray examination, the use of gastroscopy is well advised since it may demonstrate pathology that for physical reasons cannot be seen radiographically.

TABLE 2

FINDINGS IN FIFTEEN POST-GASTRECTOMY PATIENTS

X-ray indefinite and no findings	1
X-ray normal but pathology found	
Alkaline gastritis	5
Marginal ulcer	2
X-ray abnormal and pathology	
Gastric obstruction	2
Diverticulum	1
Recurrent ulcer	2
No pathology	2

Gastroscopy to follow post-gastrectomy and vagotomy patients is another extremely valuable procedure because it allows the surgeon to better evaluate his patients' status. Table two illustrates the problems encountered in the post-gastrectomy patients. Of this group there are two disease states of real significance in the followup. Alkaline-gastritis as manifest by upper abdominal pain, nausea, vomiting, anemia, weight loss, is easily seen and diagnosed by the gastroscope. Second, marginal ulcer may not be detected by x-ray examination but will be seen at gastroscopy.

The category of patients entitled "X-ray abnormal and diagnosis made by gastroscopy" are those patients with varying pathology suggested by x-ray and by an abnormal x-ray confirmed by gastroscopy. In addition, some of the x-rays which were abnormal represented studies which showed an ulcer thought to be malignant in nature and were found to be benign after gastroscopic biopsies. The last category are those patients considered to be normal in upper-gastrointestinal studies which are in fact confirmed by gastroscopy.

All in all, use of the fiberoptic gastroscope is a significant advance in diagnosis and management of patients with real or suspected upper alimentary disease.

Francis A. Barrett, M.D.
Wyoming Editor

Bioavailability of drugs*

J. Cedric Jones, M.D., Lander

One of the important aspects of therapy now and in the future is a knowledge of the parameters which alter the effectiveness and utilization of drugs.

THE BIOAVAILABILITY OF A DRUG is the relationship between the entire dose of a drug that is presented to the body, by whatever method, and that portion of the dose that finally reaches the target organ and is available to perform the duty for which it was intended. Such a definition requires consideration of the method of administration, the various factors that inactivate or delay the drug in its course to the final organ and its effectiveness, and finally its metabolism in the body and its elimination from the body.

Any drug introduced into the body must pass across many and various cell membranes before it finally acts, is destroyed, and eliminated. Most cell components such as nuclei and mitochondria have only plasma membranes, but cells themselves are surrounded by a membrane that is largely lipoid in nature, and to gain entry to the cell the drug must pass this membrane. A continuum of cells, such as the epithelial lining of the intestinal tract, provides in general a barrier to the passage of all but lipoid-soluble compounds. There are, however, very small breaks or pores in this membrane that allow the passage of small or water-soluble compounds. In the former case, passage is by simple diffusion; in the latter, it is by filtration through these small pores. The nature of the membranes determines the size of these pores—in the red cell membrane, they are in the 4 Angstrom range, and in the wall of capillaries of the 40 Angstrom size, so that small protein molecules can pass through them.

As with other tissues throughout the body, and as with anesthetic gases, the rapidity with which compounds pass the cell membrane is determined by the relative degree to which a compound is soluble in fat compared to its solubility in water. This is known as the lipoid:water or the fat:water solubility coefficient. The pH and the concentration of weak electrolytes also influence the diffusion of drugs across lipoid membranes, the former by determining the degree of ionization of a drug. Most non-ionized drugs pass lipoid membranes without difficulty, but ionized drugs do not. In case of semi-permeable membranes with pores, ions can pass either or both ways to reach equilibrium. However, if some are too large to pass, or if some non-ionized compounds do not pass, an equilibrium will be reached on the two sides of the membrane in accordance with the Donnan equation. Weak electrolytes, such as are most medicines, will distribute themselves on the two sides of a lipoid membrane, first on the basis of the non-ionized portion, and it will become equal on the two sides, as for example within the stomach and within the blood plasma across the stomach wall. The extent to which ionization will take place on the two sides of the lipoid membrane will be according to the Henderson-Hasselbach equation. In general, within the strong acid environment of the stomach, weak acids will be relatively non-ionized and subject to rapid absorption. On the other hand, weak bases will be relatively ionized and therefore not absorbed within the stomach, but will pass on into the intestine for absorption.

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*Presented before the Winter Seminar, March 1975, Cheyenne, Wyoming

Furthermore, there are certain active transport mechanisms across membranes. Active transport occurs against an electrochemical gradient and requires the expenditure of energy. Facilitated transport does not require energy but occurs more readily than simple diffusion.

Most drugs are administered orally. Drugs given by mouth are either in solid form or dissolved before they can be absorbed. Once the drug is in solution, absorption depends principally on (1) the pH of the absorbing membrane and (2) the degree of ionization of the drug. Some drugs are absorbed in the mouth, as nitroglycerine under the tongue, and from that site they are absorbed into the blood stream and become almost instantly available to the target organ, in this case the heart. However, drugs with a foul taste or an astringent action cannot be tolerated in this fashion.

The stomach presents an interesting situation in the matter of drug absorption. The gastric juice is highly acid and that fact will influence absorption. Depending on the drug's own nature as regards acidity or alkalinity, it will exist in an ionized or a non-ionized state. Drugs which are non-ionized in the acid medium are fat soluble and are readily absorbed in the stomach. There is an equilibrium between ionized and non-ionized compounds in solution. The pKa of a compound is the pH at which half the compound exists in the ionized and half in the non-ionized form. This in turn depends on the medium into which it is placed.

Many drugs are alkaloids and as such are highly ionized in the stomach and therefore are poorly absorbed. However, when they pass into the intestine, they are absorbed. This means that ephedrine, for example, given by mouth, is slowly absorbed because it must pass through the stomach and into the intestine before it is absorbed. The same would be true of morphine or atropine given by mouth. Other drugs, as for example pentothal, are salts of weak acids and at the pH of the stomach are non-ionized and rapidly absorbed.

Other factors that influence absorption include the area available for the purpose, so that much absorption will take place in the intestinal tract. The same is true of the peritoneal cavity and the pleural space for drugs instilled in these sites. In rectal administration of drugs, the venous return from the area is important. The lower rectum is drained by the hemorrhoidal veins, but higher up and throughout the stomach and intestine, blood is returned through the portal circulation. If then, one is to use rectal administration of drugs that are detoxified by the liver, they should be given in small volume so as not to be returned through the portal circulation and thus detoxified by the liver before they have an opportunity to perform as intended.

The intravenous route is another method to be considered. Drugs probably are more readily bioavailable by this route than by any other, but even here events occur that limit their effectiveness. Many drugs are highly bound by plasma proteins, principally albumen, and in such fashion are only slowly available as various equilibria occur. Butazolidin is an example that is highly protein-bound, something like 95 percent becoming combined with protein. Thiopental is another, with something like 65 to 75 percent being bound initially. Of course, such binding removes the possibility of the drug being lipoid soluble and therefore it is not available to the cell. Additionally, being bound it does not pass the kidney glomerulus. As it is released, however, depending on other factors such as pH differential of the fluid in which it is contained, lack of ionization and the like, it becomes fat soluble and active.

Protein binding also has another facet. X-ray opaque dyes can have a greater affinity for albumen than does pentothal. Thus, they can displace bound pentothal or can limit the quantity of albumen available for binding and thereby create a situation in which we might find an overdosage with pentothal.

Another factor influencing the bioavailability of drugs has to do with the distribution of drugs within the body, and in this regard the blood supply is important. A very large portion of the cardiac output is directed toward the brain, and to anesthetists this is one of the vessel rich organs which receives a large proportion of any drug given intravenously. Because thiopental is non-ionized in the plasma and because it goes to the brain in high dosage and is fat soluble, its action is prompt, but without further dosage, the thiopental is redistributed into other tissues with less blood supply. While muscles have a lesser blood supply, the mass of muscle is large and they take up much of a drug. Fat, which is a reservoir for fat soluble thiopental, is vessel poor but eventually will contain much of the drug. In fact, thiopental is not thoroughly removed from the body for many hours because of that portion dissolved in fat.

This matter of blood supply is most important in the administration of anesthetic agents. They, in the case of all the inhalation agents, are taken in through the lungs without regard for ionization or solubility. They simply pass the alveolar membrane by diffusion to reach the blood. However, if we consider that their locus of action is the neuronal synapse, the fat solubility becomes important, and most of them are fat soluble.

Subcutaneous injections are irregularly absorbed depending on various factors. If the patient is in shock and under the influence of catecholamines, he will have very little circulation to pick up and remove the drug, and it might be almost useless. There is a greater blood supply to muscle tissue, but still too little for reliable absorption in shock. On the other hand, in the case of excitement, the blood supply may be increased and the drugs picked up very readily from either subcutaneous or intramuscular injection.

Local anesthetics are frequently used under the skin. They are salts of strong acids and are water soluble. When injected into tissues, their pH is altered by the tissue fluids such that they become alkaline and the free base is precipitated to cause anesthesia. Thus, when injected around inflamed tissue with a high metabolic rate and acidosis, they are less effective. If mixed with an alkali, they become more effective because of the alkalinity.

The same applies to topically applied drugs—namely, they become more effective if they are alkaline on the surface and fat soluble. The variability of absorption from mucous surfaces should be mentioned here. Trachea, bronchi, and urethra are highly vascular and rapidly absorb topically applied anesthetics, even to the extent of causing toxic reactions. The bladder also is quite vascular, and will become a source of toxicity if the urine is alkaline rather than acid.

The status of the individual patient is most important in bioavailability because it produces variations in the utilization of drugs. Genetic backgrounds can cause different responses to drugs, as can age and sex. It is well known that the elderly tolerate drugs less well than do the young, and in some instances response can be different in males than in females. Prior use of drugs regularly, even to cigaret smoking which is known to induce liver enzymes, can vary the individual's response—likewise use of alcohol or phenobarbital. Known kidney disease may be of more import than liver disease; various water soluble drugs, as lanoxin, are eliminated by the kidney and kidney failure can lead to lanoxin overdosage. On the other hand, the liver's huge reserves of enzyme production may allow for the rapid breakdown of a drug even in liver disease.

A number of the considerations discussed above are illustrated in the product that some consider to be the ideal for the administration of aspirin. In tablet form aspirin has to extract the solvent for its solution from the gastric juice, and this creates a highly acid area immediately surrounding the aspirin tablet. This event is damaging to mucosa and capillaries, leading to bleeding. So the aspirin is given in suspension so as to be dispersed somewhat, thus lessening the acid environment and allowing for the non-ionization of the aspirin and its fat-solubility and absorption. Bleeding still remains a problem. The pharmacologists then suggest that the aspirin, in addition to being given in suspension, be given with antacid containing magnesium and calcium carbonate and magnesium oxide, but not aluminum since the latter forms a highly insoluble compound with aspirin that delays absorption. The antacid also should be in suspension. Such a preparation will create an alkaline environment, causing ionization of the aspirin and delaying its absorption into the small intestine. Under these circumstances, no bleeding has been found, and the aspirin is fully absorbed. Systemic alkalinization with sodium bicarbonate is not good since it promotes the renal excretion of aspirin by forming an alkaline urine. Urine should be kept acid to maintain plasma levels of salicylate in treating the chronic arthritic with aspirin, but it should be made alkaline in aspirin poisoning.

Summary

The purpose of this presentation is to offer some suggestions as to why a drug seems to act differently on one occasion than on another, or why it acts differently in one patient than in another. Many factors affect absorption of a drug and its distribution to the effective area. There apparently are various patient-related or genetic factors that modify bioavailability of drugs. Finally, it is suggested that there are small changes that can be brought to bear that will help in bioavailability or help in the treatment of drug overdosage.

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Vaginal prolapse:

*Colpopexy by the lateral vaginal approach**

**Walter G. Saunders, MD, Sheridan, Bohdan Kupczak, MD and
Edward A. Zimmermann, MD, Albuquerque**

Prolapse of the vaginal vault is a rare occurrence for which many operative procedures have been devised. Most operations avoid utilizing original supportive ligaments and fascia. Many sacrifice vaginal function. Lateral vaginal colpopexy combines anatomic soundness with the desirability of a vaginal approach, and vaginal integrity and function are maintained.

VAGINAL VAULT PROLAPSE FOLLOWING hysterectomy is fortunately a rare occurrence in modern gynecologic practice. In 1952 Phaneuf[11] reported a fifteen year review of his private records; of 5,554 operations only seven were for posthysterectomy vaginal prolapse. In 1960 Symmonds and Pratt summarized the Mayo Clinic experience from 1935-49 and found 69 operations for vaginal prolapse.[17] Current surgical therapy for this problem include vaginal, abdominal, and combined approaches. Many synthetic materials recently have been used,[16] and all available tissues have been employed to suspend a sagging vagina. In an attempt to preserve vaginal function multiple anatomically incorrect and surgically elaborate operations have been advocated in recent literature.

Lateral vaginal colpopexy combines the desirability of an easy and anatomically correct approach to vaginal prolapse while also providing vaginal access to conditions which may require concomitant vaginal repair. The increased morbidity of pelvic laparotomy is circumvented, the repair may usually be accomplished without opening the culdesac, and the functional integrity of the vagina is maintained. For these reasons we propose this operation as the procedure of choice when dealing with posthysterectomy vaginal prolapse either as a solitary defect or in combination with cystocele, rectocele and/or enterocele.

Technic of Operation

As with any operation, preoperative preparation of the patient is paramount to insure success. Atrophic vaginitis or active infectious processes of the vaginal canal and bladder should be treated with appropriate measures. Obviously, neoplastic changes must be ruled out by cytologic examination and biopsy as necessary. Urologic evaluation is necessary to the extent indicated by symptoms and urinary findings.

Once in the operating room it is highly advisable that indwelling ureteral catheters be placed prior to commencement of the operation. This is especially desirable in cases of multiple previous attempts at correction of massive prolapse in which the ureters may be medially displaced and in which extensive lateral dissection may be necessary in order to properly support the vagina.

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Following placement of the patient in the dorsal lithotomy position and completion of an adequate prep, even in the examination under anesthesia the attenuated ends of the uterosacral and cardinal fascial condensations lateral and posterior to the vaginal apex may not be identifiable. A weighted speculum is placed in the vaginal vault and the lateral margins of the vaginal apex identified. Usually the vaginal cuff scarred margins will approximate the proper location. Allis tissue forceps are placed one centimeter anterior and posterior to the apex at the lateral border and a triangular wedge of vaginal inner membrane approximately 3-4 cm in length can be elevated or removed by sharply undermining the edge toward the introitus (Fig. 1). The amount of this excision controls the diameter of the resultant vagina so one should be conservative when preservation of sexual function is important.

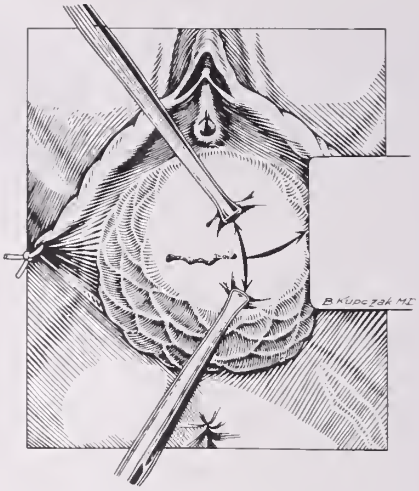

Fig. 1. Vaginal prolapse exposed with allis clamps at the left margin of the vaginal apex demonstrating the vaginal tissue to be removed.

The dissection is then carried laterally until the true substance of the cardinal and uterosacral endopelvic fascia condensations are well identified. This is best accomplished we believe by grasping with Allis forceps in a hand-over-hand technic the attenuated ends, or at least the tissue in the region of the cardinal and uterosacral ligaments. In this manner the identity of these two important structures will ultimately be delineated on either side of the pelvis. The indwelling catheters assist in identifying and demonstrating the course of the ureter by palpation during the procedure. If necessary the entire vaginal apical and culdesac areas may be opened to enhance their identification. We do not, however, routinely find it necessary to violate peritoneum unless concomitant enterocele repair is contemplated—if so, this should be accomplished now in routine fashion. Large degrees of descensus will be accompanied by more laterally displaced pedicles, while in lesser defects their identification will be simpler.

Once the ligamentous pedicles have been identified and elevated with Allis forceps, they are sutured together with three #1 chromic sutures encompassing the endopelvic fascia both anterior and posterior to the actual ligaments (Fig. 2.) These sutures are tagged for future reference and not tied at this time. The contralateral dissection is then similarly accomplished and the two most lateral sutures on each side are simply tied. The long ends of the medial sutures are rethreaded on needles and passed laterally through the fascia around each bundle created by the other sutures. This serves to tightly incorporate cardinal, uterosacral and investing contiguous musculo-fascial tissue into a solid base of support upon which the vaginal mucosa may be attached. The defects in the vagina are then closed with interrupted catgut sutures which dip well into the fascia while approximating the mucosa. If the vaginal apex has been opened it should now be closed in a manner designed to minimize shortening. Cystocele and rectocele repair may be accomplished as necessary, and the operation terminated.

Hemostatic packs are not employed, as blood loss should be well-controlled by the surgery itself. The ureteral catheters are immediately removed and replaced with an indwelling foley for twenty-four hours. A broad spectrum antibiotic or urinary anti-infective is advisable because of the ureteral trauma.

Postoperative care is similar to that for posterior colporrhaphy. We employ systemic estrogen in postmenopausal patients and utilize a topical triple sulfa creme in nonallergic individuals.

Discussion

Traditionally papers expounding surgical technic include historical sketches to provide background for their claims or to illustrate a logical sequence of development of a particular

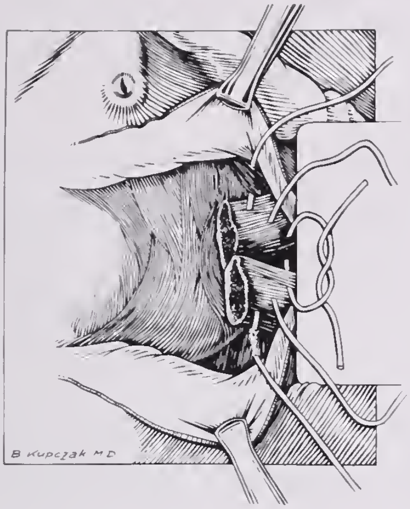

Fig. 2. Left-sided dissection is complete, utero-sacral and cardinal pedicles have been identified and are being sutured together.

procedure. For several reasons, a similar attempt seems warranted here. First operations common to the late nineteenth and early twentieth centuries are no longer performed despite enviable results considering the era. Second, the anatomic basis for this particular repair was initially described almost fifty years ago,[10] but has been little employed. One "new" technic[15] seems reasonably close in intent, and similar modifications have been recently espoused and reported.[17]

Prior to the 1880's vaginal prolapse was invariably accompanied by uterine prolapse and treated locally with pessaries, caustics and cauteries. Hysterectomy of any kind was seldom performed and vaginal procedures were adjudged to result in too much "shock" to be justified. LeFort in France and Donald (Manchester operation) attacked the problem virtually at the same time. LeFort's original and modified procedures over the years have been reserved primarily for the elderly and celibate.[5] The Manchester operation with its several modifications by Shaw, Fothergill, etc., continues to enjoy great popularity in Britain.[4] Just before the turn of the century, Watkins[20] described his "Interposition" operation and Wertheim his "Transposition." Subsequently these enjoyed considerable success in this country until the Thirties.

These procedures and the Spaulding-Richardson operation[13] all share in experienced hands the common advantage of being less traumatic than hysterectomy but the common disadvantage is retention of a potentially diseased organ. The uterus or portions of it are utilized to substitute for attenuated or absent natural supportive elements, or the preserved "keystone" (portio abdominalis of the cervix) is used as a sheet anchor to which the transplanted cardinal ligaments are attached.

By the mid-twenties vaginal hysterectomy and plastic operations came into vogue. Symmonds and Pratt[17] blame the Mayo technic[9] with its inadequate fixation of supporting ligaments to the vaginal apex for many of the failures they later treated. Norman Miller[10] in 1928 was the first to describe incorporation of ligamentous support to the vaginal apex to prevent and/or reverse vaginal descensus. His operation though anatomically sound unfortunately never achieved the favor it deserved among American Gynecologists, and it is not mentioned in current textbooks of operative gynecology.

Richardson's description of a safer method for total abdominal hysterectomy,[14] followed ten years later by the Heaney vaginal hysterectomy[6], certainly caused the demise of the interposition operation and relegated colpocleisis and vaginectomy to geriatric populations in this country. Another contributing factor favoring hysterectomy as a primary procedure of operative therapy has been the dramatic lessening of morbidity and mortality made possible by better anesthesia, improved antibiotics and safer blood replacement when needed.

Despite the emergence of gynecology as a primary surgical specialty with emphasis on vaginal surgery, abdominal approaches to uterine descensus and vaginal prolapse following hysterectomy continue to have their advocates. Grant Ward[19] espoused ox fascia lata, while Williams and Richardson[21] advocate utilization of external oblique aponeurosis as suitable material to suspend the vagina. With the advent of synthetic inert materials the approaches have become even more exotic. Soichat[16] described using a retroperitoneal silastic splint to overcome genital prolapse. Shirodkar advocated using nylon to suspend the vaginal cuff to the sacrum.

Similarly other surgeons have recently avoided seeking the original supportive elements for more easily defined, albeit less anatomically correct, structures. Falk[3] and Lane[8] attach the vaginal apex to the sacrum while Randall and associates utilize a transvaginal approach to suture the vagina to the sacrospinous ligament.[12] From the standpoint of the surgical anatomist these latter approaches make little sense. Krantz,[7] in a recent publication states that support of the upper vagina is entirely from the cardinal ligaments and lesser fascial condensations of endopelvic fascia. The lower third is supported, he maintains, by the puborectalis muscle of the levator ani group and the introitus by the bulbocavernosis muscle.

Loss of apical support results in vaginal inversion (prolapse), while herniation of peritoneum and bowel through an inadequate reconstructed vaginal cuff may result in a "cuff hernia." Weakened rectovaginal fascia results in enterocele formation when the defect occurs just below the culdesac of Douglas. Loss of support at other levels allows the vagina to evert with resultant passive accompaniment of bladder, ureters, and rectum. Others have made similar statements as to vaginal support but have emphasized other relationships such as the close approximation to the Levator Ani group as the basis for their repairs.[12]

With the above rather sketchy surgical anatomy expose as background, it becomes more evident that fascial reapproximation such as that employed in simple anterior colporrhaphy or approximation of the levators in the midline in a posterior repair does nothing to correct the higher placed defect. We feel strongly, as did Norman Miller and Te Linde[18], that reestablishment of integrity between the cardinal and other endopelvic fascia condensations and the upper vagina are prerequisites and consonant with success.

If one closely reads the report of Symmonds and Pratt[17] it appears that their operative technic is basically similar to that which we advocate. Chief difference lies in our emphasis on lateral exposure and dissection at the outset and the avoidance of removing the vaginal apex in otherwise uncomplicated cases which should minimize foreshortening. The recent publication by Segala[15] appears strikingly similar to the original Norman Miller procedure although he too relies heavily upon midline fascial approximation for primary support.

Te Linde has succinctly summarized the etiology of vaginal vault prolapse into four basic causes, the understanding of which serve to reinforce our approach and the knowledge of which should in due time eliminate the necessity of this operation being done in the majority of patients.[18]

1. Crushing the ligaments when performing a hysterectomy with resultant postoperative tissue necrosis, poor scarring, and eventual attenuation resulting in inadequate support. This is certainly less common since the "clamp" method has fallen from vogue, and is the partial basis for success of the Manchester, Richardson, and Watkins procedures which presupposed adequate ligaments untouched by surgery.

2. Failure to properly transfix the uterosacral and cardinal ligaments in total vaginal or abdominal hysterectomies. The Mayo vaginal hysterectomy is a case in point. Current attention to Heaney technic or proper placement of angle sutures in an abdominal operation should largely eliminate this cause.

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3. Failure to recognize or treat accompanying descensus at the time of original surgery. With this should go the oft-stated adage that abdominal hysterectomy is generally not the therapy for uterine descensus. Recognition of associated defects is directly related to adequate preoperative evaluation and judgment of the surgeon.

4. Senile changes in tissues that were properly supported at the time of the initial operation. Prolapse may occur years removed from the initial surgery in the presence of excessive weight gain or systemic illness. These factors and others may well exonerate the primary surgeon from being implicated in the eventual failure of the operation.

Summary

Vaginal vault prolapse following hysterectomy may arise from a variety of reasons which include poor surgical judgment and operative technic. The anatomic defect lies primarily in the disruption of the supportive attachments between the cardinal-uterosacral ligaments and the vaginal apex with the endopelvic fascia acting as the "cement" or interface between the vagina and pelvic wall. Progression of descensus causes these ligaments to retract more laterally and hence out of the plane of dissection advocated by midline approaches. Primary identification and utilization of the ligaments is difficult or impossible unless extensive lateral dissection is employed. Lastly, lateral vaginal colpopexy attempts to reestablish anatomic continuity while minimizing vaginal shortening. Its anatomic soundness makes it the operation of choice when dealing with vaginal prolapse following hysterectomy regardless of associated lower vaginal eversions or enterocele.

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Slow virus diseases*

Malvin Cole, MD, Casper

This interesting report should alert us to some uncommon but serious neurologic diseases.

THE PURPOSE OF THIS PAPER is to draw attention to an important subject in investigative neurology, namely the "Slow Virus" diseases. Although some of these diseases are in themselves uncommon, they have many theoretical implications which may involve some of the more common diseases of the nervous system. Some of the information has been suggested to clinical neurologists by our veterinary colleagues because of similarities in clinical findings, pathology, and the natural history of the disorders. Other information has been gathered by epidemiologic investigation and by newer virologic research. It should be emphasized that many of the rules of proof that exist in bacteriologic infections do not exist with virus infections. In fact the literal content of Koch's postulates probably cannot be fulfilled with viral infections, yet the overall philosophy of Koch's postulates hold and require that "sufficient evidence needs to be accumulated to make a case beyond reasonable doubt for a cause and effect relationship."[1]

The slow virus diseases of the central nervous system can be divided into two groups: The first are the Subacute Spongiform Encephalopathies, so named because of the nature of the neuropathologic findings. These are caused by "unconventional" viruses. The second group are caused by "conventional" viral agents.

The disorders due to the unconventional agents have the following characteristics: (1) lack of fever, (2) lack of inflammation, (3) lack of changes in the cerebro-spinal fluid, (4) lack of immune response, (5) lack of sensitivity to agents that inactivate conventional viruses. (6) lack of electron microscopic evidence of virus particles, (7) lack of evidence on cell cultures. Nevertheless, in spite of these characteristics, there is epidemiologic and biologic evidence that these disorders are due to viral agents. This evidence consists of transmission of infection from human to chimpanzee to chimpanzee, transmission to new world monkeys, and transmission to the domestic cat. These transmission experiments, with neuropathologic sequellae of similar nature, warrant the conclusion that the transmitted disorders are very similar if not identical to each other and that they are due to viral or viral-like agents.

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*From the Department of Neurology, Memorial Hospital of Natrona County, Casper, Wyoming. Presented before the Winter Seminar, March 1975, Cheyenne, Wyoming.

This group of diseases include the following: (1) Scrapie, a disease known for 200 years in Scotland and the northern isles which means in Scottish "rubbing on fixed objects" and consists of a progressive ataxic paralytic disorder of sheep, (2) Transmissable mink encephalopathy, which may be identical to Scrapie, (3) Kuru, and (4) Creutzfeld-Jacob Disease.

Kuru,[2,3] a term meaning tremor, occurs among the fore highlanders in New Guinea. These are a primitive people in which this cerebellar degeneration, characterized by tremor, ataxia, weakness, dysphagia, nutritional defect, inanition and fatal ending, was once the commonest cause of death among adult females. It is transmitted by ritualistic cannabalism among females and some children—a disease now being eradicated.[4] Creutzfeld-Jacob Disease is a subacute progressive dementing disorder, generally occurring in the presenium. Myoclonic jerks, at times pyramidal, extra pyramidal, cerebellar and even lower motor neuron findings are part of the disease. The disorder terminates fatally in six to twelve months. The following is a summary of a recent case with a four-month course.

CASE REPORT

K.M., a 66-year-old white male, noted vertigo in April, 1974. One month later there was truncal and limb ataxia. Two months after onset he developed confusion, disorientation, dysarthria, nystagmus, a right hemianopia to double simultaneous stimulation, and a snout reflex. He then rapidly developed dystonic posturing, perseveration, coma, and myoclonic jerks. The typical periodic EEG was not seen. Laboratory investigations were essentially normal. Findings at postmortem examination were consistent with Creutzfeld-Jacob Disease.

The second group of slow viral diseases, those due to "conventional" viral agents, depend to a large degree on an alteration on the host response. Our veterinary colleagues have shown us that a disease of sheep called Visna has many similarities to the diseases seen in humans. It is characterized by a progressive ataxia ending in death, often with an interstitial lymphocytic pneumonia and a meningeal infiltrate of inflammatory cells with peri-vascular inflammation and peri-venous demyelination. It has not been transmitted to experimental animals but is known to be caused by an RNA virus 75 to 100 microns in diameter.

Progressive Multifocal Leukoencephalopathy, another disease of this second group, has been, in most cases, associated with some abnormal immune status either due to the basic disease state such as Hodgkin's Disease[5] or other lymphomas, sarcoidosis and the like, or to treatments of these disorders which depress the immune response. There are some cases reported, however, in patients in whom these states do not exist.[6,7] Progressive Multifocal Leukoencephalopathy generally begins as a unilateral focus of hemisphere dysfunction which gradually becomes generalized and bilateral. It is usually fatal within three to six months, although a case has been reported with remissions which ended fatally after five years.[8] There is no inflammation present, and Demyelination is the pathologic change. The disease is known to be due to a papova virus either JC virus or simian 40 virus.[9]

A third disease, Subacute Sclerosing Panencephalitis, is seen in children four to eighteen years of age. The first stage is characterized by personality changes, visual disorders, choreo-retinitis, and dementia. The second stage is characterized by seizures or myoclonic jerks, progressive dementia which goes on to the third stage of stupor or coma, rigidity, autonomic dysfunction, a periodic EEG, and finally death. The course of the disease is from three months to seven years. Pathologically, there is atrophy in the central nervous system, necrosis, secondary demyelination, astrocytosis, some inflammation and intracellular inclusion bodies. The spinal fluid is abnormal in that the gamma globulin fraction is increased, and there are elevated titers to measles in both serum and spinal fluid. It is of interest that fifty per cent of these patients have a history of measles prior to the age of two years, and this disease is known to be due to a measles or measles-like virus.[10]

Implications for Common Neurologic Disorders

As mentioned previously the Slow Virus Diseases may be of importance in some of the more common neurologic disorders. A major question in neurology today concerns the importance of slow viruses in the etiology of Multiple Sclerosis.[11] The concepts that Multiple Sclerosis may be due to such infections are not mutually exclusive with those which implicate an autoimmune process. Neither may be correct (though probably one or the other is) or they both may be correct. For example there may be some abnormal immunologic response to past viral challenge. Increased titers of measles antibodies have been found in the serum[12] and also at times, in the spinal fluid, and some virus-like particles have been observed in the brain of Multiple Sclerosis patients.[13] It should be emphasized that although there is much investigation concerning slow viruses in Multiple Sclerosis and there is a good deal of suggestive evidence, at the present time their involvement is by no means proved. •

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Clindamycin in deep pharyngeal infections*

A preliminary report

G. L. Smith, MD, Cheyenne

Although serious toxic complications from clindamycin, especially colonic have been reported, this antibiotic appears to be unusually effective in certain conditions, one of these being deep pharyngeal infections.

Discussion of deep pharyngeal infection, the most common of which is peritonsillar cellulitis with and without abcess formation, appear in the literature from time to time. Each appearance is generally because the author is proposing what is felt to be the best "cure" for the condition. That these discussions continue to be presented in various medical writings, and in medical practice, in spite of great progress in the therapy of infectious disease in general, indicates that a "cure" has yet to appear. From the many and varied methods of treatment proposed by different writers, it is also apparent that the optimum course of therapy has yet to be found.

Deep pharyngeal cellulitis, principally acute peritonsillar cellulitis, is characteristically sudden in onset, often following an acute pharyngotonsillitis—but not always. Many cases seemingly begin as a deep infection particularly in the base of the tongue or in the parapharyngeal spaces. Their morbidity is greatly enhanced by the early onset of dysphagia leading to dehydration and inability to utilize oral medication. Trismus, lingual displacement of the tonsil, or edema occur early in the course of the disease. These when coupled with exquisite tenderness of the affected parts make accurate examination and evaluation difficult and at times impossible. Improper diagnosis can then lead to delay in effective treatment, further increasing the morbidity of the disease.

When abscess formation is suspected, and this is often a difficult judgement to make, surgical drainage of some type is generally advised and employed. In some instances improvement is dramatic, but such a result is by no means routine. Furthermore the potential hazards of surgery, aspiration, hemorrhage and septicemia are present in almost all instances. The dangers of the use of anesthetic agents in a toxic, febrile and dehydrated patient could be discussed at length. That so few actual problems have resulted perhaps is because these infections are generally in young, robust people (age 15-35 years) and because much extra effort is made to prevent catastrophe when surgery is done.

In the past many attempts have been made to treat these conditions with antibiotics. In commonly used dosage schedules, results of most antibiotics have been disappointing in general. Most successes have been achieved only by use of a combination of some form of surgical drainage plus antibiotic therapy, and in these instances the importance of the antibiotics is frequently open to question, equally good results having been reported with surgical drainage alone. Some increase in success was obtained with the advent of broad spectrum parenteral antibiotics such as Kantrex and Gentamicin, but the toxic side effects of these agents relegated them to near life-or-death situations and surgery remained the treatment of choice. With the introduction of cephalosporins and clindamycin it appeared that an antibiotic was available which could be given intravenously in high doses with few side effects either locally or systemically.[1]

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*Presented before the Winter Seminar, March 1975, Cheyenne, Wyoming.

Clindamycin was chosen for this study because of its seeming proven effectiveness with common pathogens of the pharynx[1,7,8] and the claim of the manufacturer that relatively high doses could be given intravenously without risk of phlebitis[4] at the site of injection and because of a reported low incidence of adverse side effects.[1,11] Since the start of this study there have been some reports of possible reversible toxicity to liver and renal systems[4,10,11] and rare but serious gastrointestinal disturbances, regardless of the route of administration. These potential toxic complications should be weighed against the advantages in the future use of this product. Very high blood levels of this agent can be obtained through the intravenous route.

Method

Only those patients presenting with disease of the pharynx that ordinarily would eventually require surgery in its management were selected for this study. The bulk of these were young adults presenting with the signs and symptoms of peritonsillar cellulitis and/or abscess. No patients known to be sensitive to penicillin were used because of alleged cross reactions between clindamycin and penicillin in sensitive patients.[1,11] Following the manufacturer's recommendation 300 mgm of clindamycin was diluted in at least 15 ml. of saline. A total of 600 mgm clindamycin so diluted was given "piggy-back" intravenously every six hours. The intravenous route was kept open with five percent dextrose in water, unless oral intake was greatly compromised by the disease and in which case routine parenteral hydration and maintenance was carried out until normal oral alimentation could be employed. This dose amounted to an average of 40mgm/kg/24 hours. Except for supportive care (analgesics, etc.) no other medications were used. The patients were informed of the study and were therefore emotionally prepared for surgical intervention should it become necessary because of lack of response of the disease to the medication. Routine throat cultures were taken on all patients upon admission to the hospital in an attempt to identify the pathogens involved.

Results

In no case was surgical intervention required. Of a total of eight patients, one of whom underwent this therapy on two separate occasions, three drained their abscesses spontaneously with subsequent rapid improvement. The other four exhibited no signs of spontaneous drainage but showed rapid clearing of symptoms and signs of illness. Of necessity the evaluation of drainage had to be subjective, and its determination was largely by close questioning of the patients who all described it as "something broke and ran in my throat". Obviously slower and less dramatic drainage could have occurred in the others and gone unnoticed.

Perhaps the most dramatic of the results obtained was the rapidity of clinical response. Most who were in moderate to severe pain and having considerable dysphagia obtained nearly complete relief in a matter of hours. The average time from the start of therapy to the relief of major symptoms (pain, dysphagia, etc.) was six hours, with the shortest being four hours and the longest twelve hours. This appeared to have little relationship to spontaneous abscess drainage or other supportive medication such as gargles. There appeared to be no variation in relation to the duration of symptoms prior to the beginning of therapy.

In the beginning of this series two patients were particularly interesting. One had been attended by another physician and presented with a classic acute peritonsillar abscess, having received large doses of penicillin intravenously without benefit. Intravenous clindamycin was then begun followed by spontaneous intrapharyngeal drainage of the abscess and relief of most major symptoms within four hours. The second patient was a female with signs and symptoms of acute peritonsillar cellulitis who was treated with parenteral penicillin and streptomycin intramuscularly followed by oral Declostatin® 300 mgm by mouth g.i.d. Declostatin was begun after no response had been obtained with the penicillin and streptomycin which had been given over a period of 24 hours. After intravenous clindamycin was started, over 48 hours elapsed before resolution of symptoms was obtained.

Throat cultures and attempts to culture those with spontaneous drainage were generally unrewarding; no specific organisms were isolated in any instance. Also, while all patients initially gave the appearance of acute toxic illness, total white count averaged 13,500 with minimal left shift. Temperature elevations were seldom more than one to two degrees Fahrenheit above normal. Temperature elevations were slower in resolving than clinical symptoms, requiring 24-36 hours to return to normal values. Part of this delay might be accounted for on the basis that almost all of these patients were moderately to severely dehydrated at the time that the therapy was begun and required at least 24 hours to correct this aspect of their dynamics.

Medication for control of pain and discomfort was ordered in each instance on an "as needed" basis, the patient having to request the medication if desired. In no instance was more than one single dose utilized and that one on admission to the hospital.

Tonsillectomy upon recovery from their acute illness was performed in two patients. One was a 14-year-old boy who gave history of recurrent episodes of tonsillitis attended by moderately severe illness, the culmination of which was this attack of acute peritonsillar cellulitis. The other was an adult female who, during this series, was treated on two occasions for acute peritonsillar cellulitis on the left side. In both instances response to intravenous clindamycin was rapid and effective, but it was felt that in order to prevent a third episode tonsillectomy should be performed. Whether or not tonsillectomies should be performed routinely in patients who have had acute peritonsillar abscess or cellulitis is still a debatable point. Probably the history of an acute peritonsillar abscess has little bearing upon the final decision of tonsillectomy except where the acute peritonsillar abscess is a proven recurrent disease. It has been our experience that recurrence of acute peritonsillar cellulitis and/or abscess is a relatively uncommon phenomenon.

Summary

A limited number of adult patients with acute peritonsillar cellulitis and/or abscess have been treated with intravenous clindamycin with an average dose of 40mgm/kg/24 hours. Response to this form of therapy has been dramatically rapid and to date has obviated surgical intervention in all cases. Two cases have required subsequent tonsillectomy after resolution of the acute disease. Relief of pain and dysphagia in a matter of four to six hours and absence of prolonged morbidity and complications have been the most striking features.

This series is yet too small to form a basis for far-reaching conclusions and further investigation is needed. From this limited experience it appears to be a safe means of treatment for a disease whose alternative form of therapy is surgical and whose surgical therapy is more hazardous, more prolonged, and more expensive to the patient. This modality of therapy reduces by more than half,the required hospital stay which accompanies surgical therapy.

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ABSTRACT OF MINUTES HOUSE OF DELEGATES

Wyoming State Medical Society
Seventy-First Annual Meeting
August 27-30, 1974
Jackson Lake Lodge
Grand Teton National Park, Wyoming

FIRST SESSION

Wednesday, August 28, 1974

The 71st Annual Meeting of the House of Delegates of the 1974 Wyoming State Medical Society was called to order at Jackson Lake Lodge, Grand Teton National Park, Wyoming, at 9:30 a.m. on Wednesday, August 28, 1974, by Dr. Paul R. Yedinak, president of the Wyoming State Medical Society. The President asked for a report from the Credentials Committee. Dr. James Stoetzel stated the Credentials Committee found everything in order and moved that the report be accepted. The motion was made, seconded and carried.

The President then declared the 1974 Annual House of Delegates Meeting of the Wyoming State Medical Society open and introduced the Speaker of the House, Dr. Ted Johnston from Cheyenne and Vice-Speaker of the House, Dr. Ross Collie from Lander.

Dr. Johnston took the podium and introduced the guests for the meeting, Senior Senator from Wyoming, Gale McGee; Junior Senator, Cliff Hansen; and Teno Roncalio, Congressman. All three gentlemen spoke on the issue of National Health Insurance.

Dr. Johnston then introduced Mrs. Liljestrand of Honolulu, Hawaii, President of the National Women's Auxiliary to the Medical Association. Upon conclusion of Mrs. Liljestrand's brief speech, Dr. Johnston introduced the Wyoming State Auxiliary President, Anne Wilson.

Dr. Malcolm Todd was then presented. Dr. Todd is the president of the American Medical Association, Associate Clinical Professor of Surgery at the University of California, Chairman of the National Advisory Committee on Health Manpower, a Regent of the newly created Uniform Services Health Sciences University, and was the United States delegate to the World Health Organization from 1970 to 1972. Dr. Todd spoke on the medical profession and problems of same and then gave a talk on his trip to China and the practice of medicine there.

Dr. Johnston introduced Dr. Jack Lewis, Chairman of AMPAC, who was to be speaker at the noon luncheon.

Dr. Johnston then announced the meeting places for the reference committees, with a brief explanation of meeting procedures.

Dr. Johnston called for new business. Dr. Flick introduced a resolution regarding the mandatory orientation program for new members of the Wyoming State Medical Society and the phasing out of same. Dr. Johnston referred the resolution to the **Research, Organization and Scientific Program Reference Committee.**

A motion was made by Dr. Flick and seconded by Dr. McCoy that the **Committee on Insurance** investigate possible substitute plans for the Blue Cross-Blue Shield coverage as is now being considered by the Medical Society. There was enough opposition that it could not be referred to the committee.

The day and time for the WYOPAC Luncheon and the Long-Range Planning Committee were announced and the exhibit booths were mentioned.

Dr. Johnston adjourned the first session of the 1974 House of Delegates at 11:50 a.m., August 28, 1974.

SECOND SESSION

Friday, August 30, 1974

The second session of the 71st Annual Meeting of the Wyoming State Medical Society, House of Delegates, was called to order by Dr. Johnston at 8:50 a.m., Friday, August 30, 1974, at Jackson Lake Lodge, Grand Teton National Park, Wyoming.

Dr. Johnston called for remarks by the President, Dr. Paul Yedinak. Dr. Yedinak read a telegram from Steven Joseph, director of the Medical Investigation for Medical Education in Wyoming, and a letter of best wishes from the president of the Nurse's Association, Joann Harnish, from Wheatland.

Dr. Johnston then introduced Bob Smith, Executive Secretary of the Wyoming State Medical Society, with the informational program on PSRO. After his discussion, Mr. Smith introduced Mr. W. C. Peck, of American Health Systems, with a further presentation of the PSRO program.

Dr. Johnston made note of an article from one of the state's newspapers containing quotations by one of our Senators and suggested that perhaps letters from members of the society were called for.

At this time, Dr. Johnston requested that nonmembers of the Medical Society leave the room.

Dr. Jim Alexander was called upon for the report of the **Medical Services Reference Committee** (MSRC) meeting of August 28, 1974. At that meeting, the **1973 Annual Meeting minutes** and the 1973 **Scholarship Loan Fund minutes** were read and approved.

Specific items, as noted, from the Council Meetings of November 18, 1973, March 13, 1974, and June 2, 1974, were read and approved.

The 1973 President's Message was read and approved.

A move was made for approval of that portion of the report. Motion was seconded and carried unanimously.

A resolution from Carbon County regarding emergency call of certain physicians was read and discussed. Committee felt this was a local option and needs no further action by the committee or the Medical Society.

The next resolution was from **Sheridan County Medical Society** regarding the shortage of physicians in certain areas of the state. Committee agrees and approves.

The next resolution was from the **Laramie County Medical Society** regarding the apparent agreement made between the State Medical Society and Blue Cross-Blue Shield several years ago, wherein the participating doctors would provide to Blue Cross case summaries on demand without compensation. The Laramie County Medical Society favored revoking this agreement. Committee recommended disapproval of this resolution. At that time, Dr. Stoetzel stated that the Executive, Governmental Affairs and Economic Affairs Reference Committee had also considered this item and there was a conflict of proposed solutions. Dr. Johnston stated they could approve the report without this resolution and then go back and record the action of the House of Delegates on this specific part of the Medical Services Reference Committee when it had been discussed later.

A motion was made, seconded and carried unanimously that the report be approved up to that point.

The next resolution resolved that the Wyoming State Medical Society vote approval of legislation empowering specifically trained morticians and funeral directors to remove donor eyes from deceased persons to be used for corneal and scleral transplants. A footnote to this resolution was that the suggested bill would specify type of training required and permission to be obtained. It was also noted that all ophthalmologists in the state have signified their approval of this program. Committee moved for approval of the resolution. Seconded and carried.

The next item was a letter from Linda Martin, project coordinator of cancer control, Comprehensive Health Planning Office, State Office Building West, concerning an HEW grant of $8,000 for a feasibility study of a cervical cancer screening project for Wyoming. The committee feels the idea is good, but has been handled poorly. The committee feels a board should be formed, consisting of an OB/GYN state member, an internist from the state, a family practice physician from the state, and appropriate ancillary people. In this way, a feasibility study for the purpose of a cervical cancer screening project could be done in an orderly and more productive fashion. A recommendation for approval was requested, at which time Dr. Nicholas pointed out there was some misinformation involved in the discussion. He stated he'd had a phone call from Stan Farrish recently and Mr. Farrish had stated that they have $11,000 for a study, and the followup then would be a grant for a three year program in PAP smear development. Dr. Nicholas stated Larry Berdelson is the person to write to concerning the Society's recommendation to establish this type of advisory board. Dr. Nicholas is sure that Mr. Berdelson will be quite receptive. Dr. Johnston requested that the secretary incorporate these changes. Motion was made, seconded, and duly carried that the report be approved up to that point.

Dr. Alexander reported that the next item considered was a presentation from Bernice Elkin, M.D., with recommendations to the **Legislative Subcommittee on Health, Education and Welfare.** The presentation was discussed but, on the request of Dr. Stoetzel, deleted because it was in conflict with another, more complete report.

Dr. Alexander reported the Physician Recognition Award recipients were approved.

There was no report on the Loss Control Panel as there were no reports from the Wyoming Pediatric Society, Wyoming Nurses' Association Liaison and Joint Practice, **Joint Practice Commission, Disability Determination Unit and/or Immunization.**

Mr. Smith requested that Dr. Kline be allowed to talk about this before the House sometime before adjournment. It was decided to bring his talk up under new business.

Dr. Alexander then moved for approval of the report with the exception of the aforementioned items. Motion seconded and duly carried.

Dr. Johnston then turned the meeting over to Dr. Ross Collie, Vice-Speaker of the House, working with Dr. Stoetzel on the report of the reference committee on **Executive, Governmental Affairs, and Economics Committee.**

Dr. Collie introduced Dr. Stoetzel, Chairman, for the report of the Executive, Governmental Affairs and Economics Committee, which met on August 28, 1974.

The **minutes of the Annual Meeting of 1973** were approved and the Committee recommended approval as printed.

The **Scholarship Loan Fund meeting of 1973** was reviewed and the Committee recommended approval as printed.

The **Council Meetings** of August 28, 1973, and November 18, 1973, were reviewed.

The Committee recommended approval of the above portion of the report. Motion seconded and carried.

Dr. Stoetzel stated that Item 10B of the August 28 Council Meeting was considered. He recommended that members pay attention to the stipend for time spent in preparation of expert testimony at depositions, giving a deposition, Court appearance, half-day Court and full-day.

The Committee recommended the following changes: That the first two items be changed from $35 per hour to $45 per hour. Item 3, half-day, $180, full day, $300.

Committee recommended and moved for approval of the above changes. Motion seconded and carried.

Mention was made of items reviewed at the Council Meeting of November 18, 1973.

The Council Meeting of March 13, 1974, was reviewed and the Committee moved for approval of that portion of the report. Motion seconded and carried.

Dr. Stoetzel stated that Item 8F of March 13 was reviewed and the Committee recommended that the President of the Wyoming State Medical Society communicate with all hospitals within the state urging utilization of their uniform billing system. Committee moved for approval of the above portion of the report. Motion seconded and carried.

Dr. Stoetzel stated, also, that Items 8G and I were reviewed, but skipped recommendation of approval of that portion of the report at that time.

Item 9A was reviewed and the Committee recommended that the President of the Wyoming State Medical Society notify the State Board of Medical Examiners that the Wyoming State Medical Society considers acupuncture a medical-surgical procedure and urges appropriate action governing the practice of acupuncture. The Committee moved for approval of the above portion of the report. After some discussion as to whether it should be worded as "experimental medical-surgical procedure," it was moved that the report be approved as submitted. Motion was seconded and carried.

Items 9B, C and 10C were reviewed.

The Council Meeting of June 2, 1974, was reviewed and the Committee moved for approval of that portion of the report. Motion seconded and carried.

Item 8A, as follows, was reviewed. Dr. Elkin reported on the **Mental Health Committee's** recommendations for legislation. After discussion, it was moved, seconded and approved that these recommendations be approved.

The Committee recommended the report be changed to the following: 1. A study has been made of mental health services in Wyoming by legislative research assistants in order to assist the Health, Education and Welfare Sub-Committee of the Wyoming Legislature to formulate new laws about mental health. 2. A position statement was approved by the House of Delegates of Wyoming State Medical Society at its meeting in Jackson in August, 1973, which reads in part: "Modern concepts of psychiatric treatment emphasize the use of community based facilities for the treatment and care of the mentally ill."

The **Mental Health Sub-Committee** therefore wishes to make the following recommendations after having studied the present law, past proposed laws, and the HEW sub-committee report.

1. Comprehensive mental health services should be provided in all regions of the state where mental health centers are functioning. These services include: inpatient, outpatient, consultation, emergency, partial hospitalization.

2. Quality control for mental health center services should be instituted.

3. It is clear to the Mental Health Committee that mental health services on a statewide basis are fragmented and dissociated. It believes that the present administrative structure leads to a division and lack of continuity of care.

4. The position of the State Hospital in terms of decreasing numbers of patients treated must be acknowledged, while also acknowledging the continuing importance of this institution. It is possible that its role might become diversified, functioning perhaps as a community mental health center for southwest Wyoming as well as an intermediate and long-term psychiatric hospital.

5. The construction of the new forensic unit at the State Hospital calls attention to the need for mental health services within the "corrections" system. This committee believes that this as well as other features of the "corrections systems" requires further examination.

6. In regard to "designated examiner" in involuntary commitment proceedings, the Mental Health Committee recognizes that there are many mental health professionals who are highly trained and competent in their field. It cannot ignore, however, the fact that functional psychiatric conditions are often mimicked by systemic diseases and that appropriate diagnostic and therapeutic measures in these instances can be instituted only by physicians. Also, if proposed patients are to be examined and detained in a hospital, they must be under a physician's care since clinical psychologists do not have admitting privileges to hospitals. For this reason, the following plan for appointing a designated examiner is suggested:

A. If there is a psychiatrist available, he should be appointed designated examiner.

B. If a psychiatrist is not available, a licensed clinical psychologist who has been certified by the examining board of the American Psychologist Association, together with a physician should be appointed.

C. If (B) is not available, a physician only should be appointed.

7. In the area of mental retardation or "developmental disabilities", the Mental Health Sub-Committee believes that an educational, rather than medical, model should be followed, preferably at a community level. Adequate medical, neurological, and psychiatric consultation should be provided, but the committee believes that emphasis should be placed on training and education.

The main thrust of this report was deletion of some of the items that were originally presented and insertion in Item 6B, the words, "who has been certified by the examining board of the American Psychologist Association."

The Committee moved for approval of the above portion of the report. Dr. Collie called for a second to the motion and asked if there was discussion.

Dr. Johnston raised a question on Item No. 7 but, after a brief discussion, it was decided the wording was adequate.

There was then some discussion about this Item (8A) being sent to the State Legislature Sub-Committee. It was decided to send it to Bernice Campbell at the Legislative Service Agency who is head of the research being done. There was no further discussion on approval of the report being sent to Bernice Campbell. All were in favor and the motion was duly carried.

Dr. Stoetzel stated the **Council Meeting** of August 27, 1974, was reviewed.

Item 7A: The Committee recommends approval of the action of the Council with the exception of adding to Item 3 of Section II of A Comprehensive Medical Education System for Wyoming, the word "future" to read, "The future development of a community hospital-oriented medical education system in Wyoming which will be designed to train medical students geared to the kind of medical practice required to meet Wyoming's health care needs."

The 1973 Presidential message and the Executive Secretary's report were reviewed and the Committee moves for approval of the above portion of the report.

Dr. Collie asked for a second to the motion, or discussion.

Dr. Loughry requested that the word "possible" be inserted so that Item 3 would refer to "The possible future development of a community-hospital-oriented medical education system."

Dr. Nicholas moved insertion of the word and the motion was duly seconded.

On further discussion of this amendment, Dr. Hunton pointed out that in the Governor's speech, he spoke positively of "the development of a community-hospital-oriented medical education system". And he asked for the Society's endorsement. After considerable discussion, it was discovered there was, unofficially, a majority of doctors in the state that would support the education system.

After further discussion, it was moved and seconded that the report state that only the first two pages of the report were approved. The amendment was carried with two negative votes. Mr. Smith clarified, for public statement purposes, that "the House of Delegates of the Medical Society approved one, two, three, as amended, and four."

Dr. Stoetzel reported that the **1975 Proposed Budget** was reviewed and Committee recommended adoption with the following changes:

1. Reduce the President's fund from $2,400 to $1,000.
2. Delete Committee expenses.
3. Delete travel expenses of the Council.

This presented a total proposed budget of $71,300. Proposed anticipated income at present is $57,475. An increase in the annual State dues to $175 would result in an income of $70,225. The Committee noted that the approval for a dues increase was made in 1969 up to $200 per year. Committee moved for approval of the above portion of the report. Motion seconded and carried.

The next section concerned resolutions.

"WHEREAS, the clerical office costs have increased markedly over the last several years,

BE IT THEREFORE RESOLVED, that Blue Cross/Blue Shield be charged the usual and customary clerical fee for application for insurability reports requiring more than a "yes" or "no" answer to the question of insurability and general health." Wording was changed to read:

"WHEREAS, the medical office clerical costs have increased."

After further discussion, Committee moved for approval of the above. Motion seconded and carried.

Dr. Hunton moved that the two statements, both of which had been covered in the report of the **Medical Services Reference Committee**, be deleted. Motion seconded and carried.

Resolution from Carbon County was considered and Committee recommended approval of Council action taken on June 2, 1974. Committee moved for approval. Motion seconded and carried.

Dr. Stoetzel presented a resolution on skiing.

"WHEREAS, aerial ski acrobatics and stunts on skis have produced many serious injuries,

BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society protest the promotion and encouragement of such activities by the ski industry in the state of Wyoming."

After discussion, the resolution was amended to delete the words "and stunts on skis".

Motion was made to accept the resolution as amended, seconded and carried with one negative vote.

At this time, the meeting was interrupted for remarks by Mr. Pecorino and Mr. Christiansen, concerning the crisis in professional liability insurance facing the Wyoming State Medical Society.

Dr. Stoetzel continued with resolutions.

"WHEREAS, the political climate is rapidly changing, and WHEREAS, there is confusion among members of the Wyoming State Medical Society as to the organization and activity of WYOPAC,

BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society House of Delegates evaluate the purpose and direction of WYOPAC and communicate its findings to the general membership."

The resolution was changed to specify that the Council was directed to accomplish the above. Motion for approval was made, seconded and carried.

"WHEREAS, severe deficiencies concerning the insurance coverage of pregnant women and unborn and newborn infants exist,

BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society communicate with the Wyoming Insurance Commissioner as to what action can be taken to improve insurance coverage of this group."

Committee recommended and moved for approval of above resolution. Seconded and carried.

"WHEREAS, a model abortion bill has been developed by the Ad Hoc Committee of the Wyoming State Medical Society, and

WHEREAS, the need for such legislation may become necessary for adequate medical criteria for performance of abortion, BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society introduce said bill if deemed necessary by the Legislative Committee."

Motion for approval seconded and carried.

"WHEREAS, the present Wyoming State Statutes concerning viability of the fetus places Wyoming in an unfavorable position statistically,

BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society propose an amendment to the present statutes changing the legal viability age from twenty weeks to twenty-four weeks."

Motion was made for approval of the above and, after discussion, seconded and carried.

"WHEREAS, certain Wyoming communities are experiencing severe health care delivery problems due to lack of practicing physicians,

BE IT THEREFORE RESOLVED, that the Wyoming State Medical Society actively supports recruiting efforts of these communities."

Motion for approval seconded and carried.

Dr. Stoetzel stated the next portion of the report was on the **Committee on Task Force Reports.** Nominees for Blue Shield Board of Trustees. Committee feels nominees are extremely vital and should exercise more control in selection of same. Therefore, Committee recommended only one nomination for each vacant position.

Motion for approval seconded and carried.

Committee recommended acceptance of all reports put before the delegates, and so moved. Motion seconded and carried.

The Committee recommended that all of the reports presented to those in attendance, be approved and moved for same. Motion was seconded and carried.

Committee recommended that the **Insurance Committee** of the Wyoming State Medical Society request competitive bids for comprehensive medical insurance coverage for the Society from other insurance companies and report to the next Annual Meeting of the House of Delegates.

A motion was made for approval, seconded and carried.

Committee requested referral of the Disabled Physicians' Act and the proposed Wyoming Nurses' Practice Act revision to the Legislative Committee.

Committee requested referral of the proposed "Code of Cooperation" between the news media and physicians to the **Long-Range Planning Committee.**

Committee requested referral of the proposed Workmen's Compensation Act to the **Workmen's Compensation Committee** for immediate study.

Committee recommended delayed action on the American Lung Association's request for the Wyoming State Medical Society to sponsor an interagency council on smoking and health until further information is presented to the Public Health Committee by the American Lung Association, and the Public Health Committee's report is received.

Committee recommended and moved for approval of the above portion of the report. Motion duly seconded and carried.

The Chair then called upon Dr. Pat Nolan, Chairman of the **Research, Organization, and Scientific Program Reference Committee,** for his report.

Dr. Nolan reported that the Committee was called to order by himself, with Dr. Erickson and Dr. Carnahan present. The following items were discussed:

The **1973 Annual Meeting minutes,** first session of August 29, 1973, second session of August 31, 1973, were read and approved by the committee.

The **Student Loan Fund minutes** were noted and approved with the recommendation that future reports include planned date to begin remuneration to the Society.

Minutes of the Council Meeting of August 28, 1973, were noted. Item 3, concerning increased funds to the Auxiliary and Item 4, the Treasurer's Report, were approved. Items 6A, F and G of the Executive Secretary's report were noted and approved. Items 8A, 9B, E and F were approved.

From the Council Meeting of August 31, 1973, Item 1 was noted and approved.

Items 3, 4A, 5A and B, 6B and 7B1 from the Council Meeting of November 18 were noted and approved. Items 10F, G, and L from the Executive Secretary's report were read and approved.The survey conducted by the **Time and Place Committee** was noted and report approved, as was the Treasurer's Report.

Motion was made for approval of the above portion of report. Motion seconded and duly carried.

From the **Council Meeting of March 13, 1973,** Items 3A and B from the President's report, the Treasurer's report, the Executive Secretary's report and the membership report were noted and approved.

From the Council Meeting of June 2, 1974, Items 3G, the **Long Range Planning Committee's** recommendations to the Council; the Treasurer's report; Item 5B of the Executive Secretary's membership report; and Items C and H of the Executive Secretary's report were all read and approved.

The 1973 President's message and the reports of the Executive Secretary and the Secretary were noted and approved, with a commendation to Dr. Mahnke for an excellent job as President.

Motion was made for approval of the above portion of report. Motion seconded and carried.

The reports of the **Long-Range Planning Committee** were accepted.

Dr. Nolan stated that a letter has been received from the **Laramie County Medical Society Library Committee** pertaining to the failure to obtain various medical journals from their jobber, Steckert and McMillan. Upon motion duly made, seconded and carried, it was agreed that the staff would collect additional information from other medical librarians in the state.

Dr. Nolan stated that subscription rates for the *Rocky Mountain Medical Journal* are increased from $3.50 to $6.00. Motion was made, seconded and approved to accept that portion of the report.

Dr. Nolan reported that a Constitution and By-law change has been proposed by Dr. Flick of the Laramie County Medical Society, and recommended to the reference committee by the Wyoming State Medical Society Council. The resolution is as follows:

It is moved that the mandatory orientation program for new members of the Wyoming State Medical Society should be phased out. This can be done by the following changes in the Constitution:

Article IV—Membership. Chapter I—Membership. Deleting Subsection (h) and by the following changes in the By-laws: Chapter I, Section 1. Delete the last sentence "For membership, he must have complied with Section 15, Chapter I of the By-laws."

Section 6. Delete "and provisional members" ending the sentence "inactive and members-at-large."

Section 7. Delete "and have complied with Section 15 of this chapter." End the sentence "of this Society."

Section 15. Delete this entire section.

Section 16. Renumber this section as "Section 15."

The committee recommended this change in the Constitution and By-laws as read. After some discussion, motion was made, seconded and carried to change the Constitution and By-laws as read.

That being the conclusion of the report, Dr. Nolan made a motion that the report be accepted in its entirety. Motion seconded and carried.

Next on the agenda was special committee reports. The **Grievance Committee** had five letters.

Dr. Kline, as Chief Medical Consultant to the **Disability Unit of the Social Security portion of the State Government,** addressed the meeting on problems in that field.

Dr. Johnston then commented on the **President's address** and complimented Dr. Yedinak on his excellent work as President for 1974.

Dr. Hunton, of the **Time and Place Committee,** gave a brief rundown of the pros and cons of the meeting place for the annual convention. A motion was made that next year's meeting be held at Jackson Lake Lodge the 26th through the 29th of August. Motion seconded and carried.

The **Nominating Committee** then named the following individuals to be voted upon for officers for the 1975 term:

President-Elect	Patrick D. Nolan, M.D.
Vice-President	James E. Stoetzel, M.D.
Secretary	Kent T. Christensen, M.D.
Treasurer	James R. Alexander, M.D.
AMA Delegate	Fenworth M. Downing, M.D.
AMA Alternate	John J. Corbett, M.D.
Speaker of the House	Theodore L. Johnston, M.D.
Vice-Speaker	Ross J. Collie, M.D.
Blue Shield Board	Gerald W. Rounsborg, M.D. Walter C. Schmid, M.D. James W. Barber, M.D.

Donald Hunton to automatically advance to President.

Motion was made to close nominations and cast a unanimous ballot for the slate of officers. Motion seconded and carried unanimously.

It was announced that there would be a Council Meeting immediately following the meeting.

The meeting of the House of Delegates of the Wyoming State Medical Society was adjourned at 12:05 p.m. on August 30, 1974.

COLORADO

Farrington Re-elected

John F. Farrington, MD, Boulder, Colorado, was re-elected to the Board of Trustees of the American Society of Internal Medicine during its Annual Meeting May 1-4.

The 49-year-old internist has been in private practice in Boulder since 1956 and is assistant clinical professor of medicine at the University of Colorado.

Dr. Farrington, a past president of the Colorado Society of Internal Medicine (CSIM) and the Boulder County Medical Society, is currently ASIM's Medical Liability Committee chairman and commissioner of the Medical Liability Commission. In addition, he has served as associate medical director of the Colorado Foundation for Medical Care, chairman of the CSIM Peer Review Organization and has been a member of the special review committee for the Experimental Medical Care Review Organization (EMCRO).

A native of Colorado, Dr. Farrington received his BA from the University of Colorado in 1949 and his MD degree there in 1952. As a Fellow of the American College of Physicians and the American College of Chest Physicians, he is active in the field of respiratory care and pulmonary diseases.

* * *

Gramlich Receives Recognition

John B. Gramlich, MD, clinical professor of surgery, University of Colorado School of Medicine, received the University Recognition Medal during the general CU commencement exercises May 23 in Boulder, for "his unremitting service, his distinguished achievements in surgery and his leadership in improving patient care and medical education in the Rocky Mountain states."

Beginning as an assistant clinical professor of surgery in 1947, Dr. Gramlich has commuted regularly from his home in Cheyenne to Denver to teach CU medical students, interns and residents. In his own state, he has worked to upgrade the quality of surgery and medicine through both local and national organizations and committees.

Lung Assn. Honors Kelble

The American Lung Association of Colorado has announced that David L. Kelble, MD is the recipient of the 1975 James J. Waring Award. The Award recognizes the "outstanding efforts and achievement of an individual contributing to the prevention and control of lung diseases in Colorado." Dr. Kelble was the 1967-68 Chairman of the Lung Association Committee which formulated the then revolutionary Glenwood Springs Prevalence Study which attempted to correlate cigarette smoking and lung disease, by survey and examination.

He presently serves as the Medical Representative to the State Air Pollution Control Commission. As Chairman of the Commission's Standards Advisory Committee, Kelble assisted in the 1974 Eisenhower Tunnel Carbon Monoxide Study. The Study recommended limits of exposure to carbon monoxide for travellers in the Eisenhower Tunnel.

* * *

Hoehns Receive Honors

Drs. Robert and Margaret Hoehn, husband and wife who are both at the University of Colorado Medical Center, were recently honored. Dr. Robert Hoehn, associate professor and chairman, Division of Plastic and Reconstructive Surgery, was elected president of the Rocky Mountain Association of Plastic and Reconstructive Surgeons. An assistant professor of neurology, Dr. Margaret Hoehn was elected a fellow of the American College of Physicians.

Dr. Robert Hoehn, who received his MD degree from Washington University, St. Louis, Mo., came to UCMC in 1970 from Columbia University College of Physicians and Surgeons, New York City. He has written more than 25 technical articles, and is the continuing editor of the section on transplantation for the *Yearbook of Plastic and Reconstructive Surgery*.

He belongs to more than 15 professional organizations and societies. For example, he is a charter member of the International Transplantation Society, a fellow of the American College of Surgeons, and a member of the Western Trauma Society, American Burn Association, American Association of Plastic Surgeons, and the Educational Foundation of the American Society of Plastic and Reconstructive Surgeons.

Dr. Margaret Hoehn, who also has written more than 25 technical articles, received her MD degree from the University of British Columbia, Vancouver. Prior to coming to UCMC, she was an assistant professor of neurology at Columbia University.

In addition to the American College of Physicians, she is a fellow of the Royal College of Physicians and Surgeons (Canada), and a member of the Association for Research in Nervous and Mental Disease, American Medical Association, American Academy of Neurology, and other professional organizations.

Butterfield Assists

L. Joseph Butterfield, MD, Director of the recently expanded Newborn Center at The Children's Hospital, Denver, has been named Assistant Representative to the Pediatric Section of the American Medical Association, responsible for the Pediatric Program for the Annual Convention of the AMA in Atlantic City, New Jersey.

* * *

Braude Named

Robert M. Braude, associate librarian of Denison Memorial Library, was approved May 1, 1975 April 26 as director of the Library. Before coming to Denison, Braude worked in the UCLA Biomedical Library Center for the Health Sciences. He received his BA and MA in psychology and a master's in library science from UCLA.

MEDICAL SCHOOL NOTES

CU Honors Convocation

The University of Colorado School of Medicine student honors convocation, presentation of Kaiser Permanente teaching awards and the Alpha Omega Alpha lecture, was held on May 16.

Dr. Gordon Meiklejohn, professor and chairman of the CU Department of Medicine, gave the Alpha Omega Alpha lecture.

Dr. Paul Seibert, associate professor of radiology, received the Kaiser Permanente Foundation award as the best clinical teacher, and Dr. John Willson, associate professor of anatomy, was given the foundation's award as the best basic science teacher.

Twenty-seven students received awards for service and scholarship. In addition, 14 seniors, eight juniors and one faculty member were announced as new members of Alpha Omega Alpha, honorary medical society. Dr. Harry Ward, medical school dean and acting vice president for health affairs, presided.

The awards and the recipients are as follows:

—Dean Maurice H. Rees scholarship for outstanding scholarship and character, Stephen E. Follansbee, Sacramento, Calif;

—Gottesfeld Memorial Prize for outstanding attainment in the basic sciences, John M. Brown, Denver;

—Lange awards for excellent performance: Steven M. Archer, Westminster, and William K. Ward, Denver, freshmen; Priscilla B. Short and David B. Witkin, both from Denver, sophomores; Caroline M. Gellrick, Ridgewood, N.J., and Keith S. Meredith, Denver, juniors;

—Roche award to an outstanding sophomore student, Richard D. Mountain, Miles City, Mont.;

—Upjohn Achievement award for outstanding academic achievement by a junior student, Richard I. Peterson, Denver;

—CIBA award for outstanding community service as an extracurricular activity, Stephen E. Follansbee, Sacramento, Calif.;

—Archibald R. Buchanan award of Nu Sigma Nu to an outstanding freshman medical student, Helen J. Gordon, Aurora;

—Woman's Auxiliary to the Denver Medical Society award for outstanding performance: Darrell G. Kirch, sophomore, and Lanny B. Reimer, junior, both from Denver;

—Edward G. Stoiber award to outstanding junior medical student, Richard O. Hammond, Idaho Falls, Idaho, and JoAnn Wells, Colorado Springs;

—Alpha Omega Alpha award for the highest attainment in anatomy by a freshman medical student, Marian D. Scott, Boulder;

—Carbon Gillaspie award for proficiency in anatomy, Carol J. Blackard, Maywood, Ill.;

—C. Walter Metz award for excellent performance in anesthesiology by a junior student, Bernard R. Pacini, Grand Junction;

—Robert C.Lewis award for proficiency in biochemistry, Jerry S. Miklin, Denver;

—James J. Waring award of Nu Sigma Nu for diligent scholarship and devotion to duty in the field of internal medicine, Bernard R. Pacini, Grand Junction;

—Chester H. Elliott Memorial award for proficiency in pathology, Craig H. Van Schooneveld, Denver;

—Richard M. Mulligan award for proficiency in pathology, Mary Beth Harris, Loveland;

—Edward R. Mugrage award for proficiency and sustained interest in clinical pathology, Tony B. Golden, Steamboat Springs;

—Robert H. Felix award for best thesis in connection with freshman work, Edwin Chappabitty Jr., Lawton, Okla., and Brian T. McGuire, Aurora;

—Franklin P. Gengenbach award for outstanding performance in pediatrics by a junior student, Paul D. Winchester, Bozeman, Mont.;

—Gold Reflex Hammer award for scholastic excellence in neurology, Mark H. Gardenswartz, Denver, and

—Richard Whitehead award of Phi Rho Sigma for superior performance in pharmacology, James R. Lingle, Denver.

* * *

Emergency Care

With financial support from the U.S. Department of Health, Education and Welfare, the University of Colorado Medical Center is sponsoring and conducting a course on "Emergency Care of the Critically Injured." Approximately 1,000 physicians in Colorado will be reached during the next two years. The course will be taught in 20 communities. The first course was given early in April in Brighton. The next one was held May 14-15 at the La Junta Medical Center, La Junta.

The course covered the entire spectrum of emergency care, including treatment at the accident site and en route to and in the hospital.

THE
BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

The Anatomy of the Ocular Adnexa: Frederick A. Mausolf, Thomas, 1975. 49 p. $4.95.

Atlas of Flexible Bronchofiberscopy: Shigeto Ikeda, University Park Press, 1974. 230 p. $75.00.

Atlas of Orthopaedic Surgery: Louis A. Goldstein, Mosby, 1974. 2 v. Gift of the Rocky Mountain Orthopedic Society.

Histology: Arthur W. Ham. 7th ed. Lippincott, 1974. 1006 p. $24.75.

Psychiatry in Primary Care: Remi Cadoret and Lucy J. King, Mosby, 1974. 339 p. $16.00.

Strokes: E. C. Hutchinson, Saunders, 1975. 283 p. (Major problems in neurology, v. 4)

Supply of Health Manpower; 1970 Profiles and Projections to 1990: Health Resources Administration, U.S. Department of Health, Education and Welfare, 1974. 222 p. Gift.

Surgery of the Upper Respiratory System: William W. Montgomery, Lea and Febiger, 1971-3, 2 v. Gift.

Surgical Diseases of the Chest: Brian B. Blades, ed. 3rd ed. Mosby, 1974. 818 p. $42.50.

Textbook of Pediatrics: Waldo E. Nelson. 10th ed. Saunders, 1975. 1876 p. $30.00.

Trauma Management: Edwin F. Cave, John F. Burke and Robert J. Boyd. Year Book, 1974. 1237 p. $77.50.

Book Review

Intensive and Rehabilitative Respiratory Care: Thomas L. Petty, MD, Lea & Febiger, 1971. 294 p., $9.75.

The era of modern respiratory care began about ten years ago with the easy availability of arterial blood gas determinations. Thereby, the Pulmonary Physiology Laboratory was brought to the bedside, and the way was then paved for precise management of respiratory failure and the optimum use of the new volume ventilators. Monitoring of the administration of oxygen both in-hospital and on an ambulatory basis became practical. No one has been more involved or contributed more to these developments than Dr. Thomas Petty whose observations and experience are summarized in this book.

This small but comprehensive book encompasses all phases of respiratory care, including Dr. Petty's major contributions to ambulatory and home care

(Chapter 15). His primary dedication to patient care, especially the patient with chronic lung disease, is evident throughout.

The intent of this book as expressed by the author is "To show how respiratory failure may be efficiently managed in general hospitals and how practical care can be applied at the bedside". He stresses the organized team approach to respiratory care, and this book is written at a level to be understood by all members of the team from the attending private physician to the house officer to the visiting nurse.

This is primarily a clinical, patient care, how-to-recognize-and-do-it book. It provides a non-pulmonary specialist with the information he needs to recognize and treat patients with respiratory failure. The appendixes, especially Sections C, "Procedure for Tracheostomy Suctioning," D, "General Recommendations for Control of Contamination of Inhalation Therapy Devices," and E, "Equipment Inventory for Respiratory Care—Inhalation Therapy Service" are most helpful in this regard, providing practical information which is usually acquired only by great expenditure of time and effort. Those interested in sophisticated and/or detailed discussions of pulmonary physiology should look elsewhere, although the ten page synopsis of pulmonary physiology written by Dr. Giles Filley and the chapter (5) on acidbase and electrolyte problems in respiratory failure written by Dr. Boyd Bigelow are excellent.

There are ample references for those who wish to read more about this rapidly developing and clinically very relevant field.

Philip R. Corsello, MD, FCCP

OBITUARIES

Wyoming

Lial S. Anderson, MD, died in Saint Luke's Hospital, Denver, on Sunday, May 11, 1975 following brain surgery.

Born in Fort Collins, Colorado, August 16, 1906, he attended the University of Iowa for his premedical requirements, then the Medical School of Northwestern University from which he was graduated in 1932. He served an internship at Colorado General Hospital, then practiced two years at Kremmling, Colorado.

In 1934 he moved to Worland, Wyoming, where he practiced general medicine and surgery for 28 years. In 1972 he retired from practice, and moved to Rancho Bernardo, California. In 1974 he moved back to Colorado, and joined a group practicing in Denver.

In 1932 Dr. Anderson was married to Alice Rodamor in Golden, Colorado. Mrs. Anderson survives as do two daughters, Mrs. Sue McGarvin, Laramie, Wyoming, and Mrs. Pat Kaiser, Waco, Texas, as well as a son, Lanny, Corona, California. Two brothers, two sisters, and thirteen grandchildren also survive.

Colorado

The death in September, 1974, of **Frances Dworak-Ryder, MD,** has just come to our attention. Born in Colorado Springs, November 12, 1893, she received her preliminary education in the public schools of that city, then attended Colorado College, graduating magna cum laude in 1918.

She then attended the University of Michigan School of Medicine, receiving her MD in 1922. After an internship at Milwaukee Children's Hospital, Milwaukee, Wisconsin, she opened an office in the First National Bank Building in Colorado Springs.

In 1923 she was married to James Ryder, who died in 1942. Following her husband's death, she entered the U.S. Indian Service, serving in the hospitals at Shiprock, New Mexico and Fort Defiance, Arizona. She left the Indian Service after the end of World War II, and opened a practice in Denver, then later in Lakewood.

She belonged to the Denver County and Colorado Medical societies, and to the American Medical Association. Formerly she belonged to the El Paso and Clear Creek societies.

She was a Life Emeritus member of the staff of Denver General Hospital, and belonged to the Associate Staff of St. Anthony's Hospital. Dr. Dworak-Ryder retired from active practice several years ago.

* * *

Recently we learned of the death in October 1974 of **Marie Ortmayer, MD,** Littleton, Colorado. She was born in Chicago, Illinois, April 2, 1884. After completing her premedical work at the University of Chicago, she entered Rush Medical College, receiving her M.D. in 1917. Following an internship at Cincinnati General Hospital, she continued graduate training at Chicago's Presbyterian Hospital, Saranac School of Tuberculosis, and in Vienna, Austria.

Save for the Saranac experience, the majority of her training was in the field of Gastroenterology. In 1932 she studied gastroscopy under Dr. Rudolf Schindler at Billings Hospital, Chicago. She was an Assistant Clinical Professor on the faculty of the University of Chicago School of Medicine.

She was a Phi Beta Kappa, belonged to the Sigma Xi scientific fraternity, and the Alpha Omega Alpha honorary medical fraternity.

She came to Colorado in 1955, and joined the faculty of the University of Colorado as lecturer, an appointment she retained until 1963.

She was a member of the Arapahoe County and Colorado Medical Societies and of the American Medical Association. She was a Fellow of the American College of Physicians, a member of the American Gastroenterological Society, the American Gastroscopic Society (President, 1955), the American Medical Woman's Association, and the American Diabetes Association.

At the time of her death she had been a resident of Carmel, California.

72nd Annual Meeting
WYOMING STATE MEDICAL SOCIETY

Jackson Lake Lodge, Moran, Wyoming

Tuesday, August 26 to Friday, August 29, 1975

TUESDAY, August 26

Specialty meetings

WSMS Gold Tournament

1st Annual Wyoming AAFP Dinner

WEDNESDAY, August 27

Remarks by Wyoming Congressional Delegation

Remarks by Max Parrott, MD, AMA President

House of Delegates

Reference Committee Meetings

THURSDAY, August 28

Scientific Session:

Introductory overview of immunoglobulins, T and B lymphocytes, humoral vs. cellular immune responses and complement.

John Leddy, MD
Division of Immunology
University of Rochester School of Medicine and Dentistry
Rochester, New York

Allergy, including IgE-mediated reactions, newer concepts of asthma and its treatment, drug reactions (especially penicillin) and probably hypersensitivity pneumonitis

John Condemi, MD
Division of Immunology
University of Rochester School of Medicine and Dentistry
Rochester, New York

Immunologic concepts in cancer and cancer therapy

Jordan Gutterman, MD
Division of Experimental Therapeutics
M.D. Anderson Hospital,
Houston, Texas

Concepts of immune complex disease including glomerlonephritis and various types of visculitis

Edmund Lewis, MD
Department of Medicine, Renal Unit
Presbyterian-St. Luke's Hospital
Chicago, Illinois

Selected auto-immune hematologic disorders. Auto-immune hemoly anemia, ITP drug induced hemolytic anemia, and thrombo cytogenia.

Dr. Leddy

Immunodeficiency diseases in children and adults: defects in humoral and/or cell-mediated immunity, leukocyte functional defects, etc.

Dr. Condemi

Panel: Immunosuppressive and anti-inflammatory drugs: Mechanisms of action and complications.

All speakers

President's Annual Banquet
Speaker: The Honorable Edward Herschler,
Governor of Wyoming

Physician of the Year Award

FRIDAY, August 29

House of Delegates: Action on malpractice insurance

Presentation of new Wyoming Blue Cross Fee Schedule

Election of WSMS Officers, Nomination of Blue Shield and Blue Shield Trustees

The above is a preliminary schedule. Exact schedule will appear in the August issue.

MEETINGS

American Academy of Family Physicians

18TH ANNUAL RUIDOSO SUMMER CLINIC

Ruidoso, New Mexico

July 14-17, 1975

Contact: Bob Reid, P.O. Box 456, Sunland Park, New Mexico 88063.

American Cancer Society,
Colorado Division, Inc.

ROCKY MOUNTAIN CANCER CONFERENCE

Brown Palace Hotel, Denver

July 18-19, 1975

Contact: American Cancer Society, Colorado Division, Inc., 1809 East 18th Avenue, Denver 80218.

American Psychiatric Association-
American Psychological Association

PERSONAL VALUES IN PROFESSIONAL PRACTICE

The Stonebridge Inn, Snowmass-at-Aspen, Colorado

July 30-August 2, 1975

Contact: American Psychiatric Association, 1700 18th Street, NW, Washington, D.C. 20009.

American Society for Surgery of the Hand

INTERNATIONAL SYMPOSIUM OF HAND SURGERY

The Lodge, Vail, Colorado

July 21-25, 1975

Contact: John A. Boswick, Jr. MD, 4200 East 9th Ave., Denver, Colorado, Container #2414, 80220.

Colorado Psychiatric Society

MIDSUMMER MEETING

Snowmass-at-Aspen, Colorado

July 25-27, 1975

Contact: Shirlee Myers, 1601 East 19th Avenue, Denver, Colorado 80218.

University of Colorado School of Medicine,
Continuing Medical Education

PEDIATRICS

Given Institute of Pathobiology,
Aspen, Colorado

July 27-30, 1975

DERMATOLOGY

Given Institute of Pathobiology,
Aspen, Colorado

July 31-August 2, 1975

CLINICAL GASTROENTEROLOGY: CURRENT TOPICS AND CONTROVERSIES

The Gant, Aspen, Colorado

August 4-8, 1975

ORTHOPAEDICS FOR THE FAMILY PHYSICIAN

The Gant, Aspen, Colorado

August 13-16, 1975

PATHOLOGY IN PEDIATRICS

Given Institute of Pathobiology
Aspen, Colorado

August 28-31, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

American Academy of Orthopaedic Surgeons

PREVENTION AND TREATMENT OF ORTHOPAEDIC WOUND INFECTIONS

August 7-9, 1975

Contact: J. Philip Nelson, MD, 1707 East 18th Street, Denver, Colorado 80218.

New Mexico Heart Institute

FOURTH ANNUAL SANTA FE CARDIOLOGY SYMPOSIUM

The Santa Fe Hilton,
Santa Fe, New Mexico

August 8-9, 1975

Contact: Santa Fe Cardiology Symposium, c/o Presbyterian Hospital Center, Albuquerque, New Mexico 87106.

SECOND ANNUAL ASPEN MUSHROOM CONFERENCE

Hotel Jerome, Aspen, Colorado

August 11-15, 1975

Contact: Aspen Mushroom Conference, 3300 South Wabash Court, Denver, Colorado 80231.

Montana-Wyoming Chapter of the American College of Surgeons

ANNUAL MEETING

Sojourner, Teton Village, Jackson, Wyoming

August 23-25, 1975

Contact: Elmer Kobold, MD, 1230 N. 30th, Billings, Montana 59101.

American College of Cardiology

TUTORIALS IN THE TETONS (Cardiac Emergencies)

Jackson Lake Lodge, Moran, Wyoming

August 23-25, 1975

Contact: University of Nebraska Medical Center, Omaha, Nebraska.

PUBLICATION PRINTING...

NEWSPAPERS • MAGAZINES
ANNUALS • QUARTERLIES
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2177 W. 7th DENVER 892-0166

American Society of Anesthesiologists

REGIONAL REFRESHER COURSE

Jackson Lake Lodge, Moran, Wyoming

August 30-31, 1975

Contact: American Society of Anesthesiologists, Inc., 515 Busse Highway, Park Ridge, Illinois 60068.

International Union Against Cancer

SECOND UICC TRAINING COURSE IN CANCER RESEARCH

The Netherlands Cancer Institute,
Sarphatistraat 108,
Amsterdam 1004, The Netherlands

September 7-20, 1975

Fitzsimons Army Medical Center
Pulmonary Disease Service-Allergy-Immunology Service

28TH ANNUAL SYMPOSIUM ON PULMONARY DISEASE

Fitzsimons Army Medical Center, Denver

September 8-12, 1975

Contact: Roald A. Nelson, MD, Fitzsimons Army Medical Center, Denver 80240

American College of Physicians
Montana-Wyoming

ANNUAL REGIONAL MEETING

Jackson Lake Lodge, Jackson, Wyoming

September 12-13, 1975

Contact: Allan L. Goulding, MD, P.O. Box 2555, Billings 59103

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FOR SALE. Sanborn Visco cardiette electrocardiograph machine. Good working order. $350.00 or best offer. Call: (303) 761-3436. 675-12-3B

PHYSICIAN WANTED. Man or woman. If you are looking for a change in your life style, then collaborate with a Ph.D. Molecular Biologist in research or Medical Services. Long-term association contemplated. Phone evenings and weekends collect, between 8 p.m. and 11 p.m.: (212) 675-7398 or Write: Ronald Friedman, Ph.D., P.O. Box 261, Bronx, New York 10463. 775-5-6B

CONSULTING PSYCHIATRIST needed by social service agency with emphasis in personal growth and vocational counseling. 4-8 hours per week as arranged. Must have experience in alternative treatment modes and group work. Send resume to Ms. Nancy Stone, Jefferson County Manpower Administration, 7625 W. 5th Avenue, Lakewood, Colorado 80226. 775-4-1B

EMERGENCY ROOM position wanted in Rocky Mountain region. 31-year old, married, Board certified internist with much ER experience. References upon request. Send details to: Eric K. Glanzer, MD, Box 1246, LaGrande, Oregon 97850, or call: (503) 963-3577. 775-3-1B

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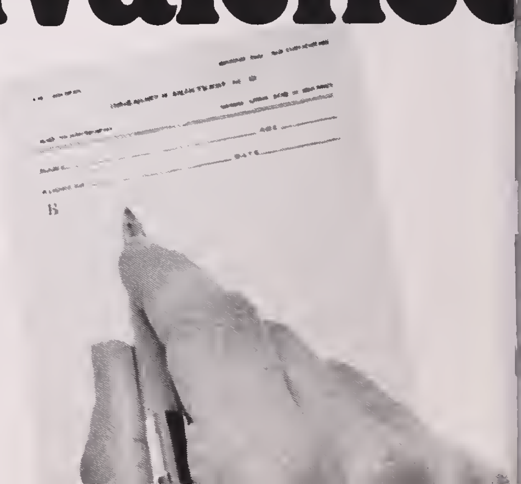
Bioequivalence



the weight of scientific opinion:

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Here are a few definitive statements in the O.T.A. report:

"...the problem of bioinequivalency in chemically equivalent products is a real one. Since the studies in which lack of bioequivalence was demonstrated involved marketed products that met current compendial standards, these documented instances constitute unequivocal evidence that neither the present standards for testing the finished product nor the specifications for materials, manufacturing process, and controls are adequate to ensure that ostensibly equivalent drug products are, in fact, equivalent in bioavailability.

DRUG
BIOEQUIVALENCE

A REPORT OF THE
OFFICE OF TECHNOLOGY ASSESSMENT
DRUG BIOEQUIVALENCE STUDY PANEL

"While these therapeutic failures resulting from problems of bioavailability were recognized and well documented, it is entirely possible that other therapeutic failures and/or instances of toxicity that had a similar basis have escaped attention."

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(a) chemical equivalence; and

(b) biological equivalence, where bioavailability test methods have been validated as a reliable means of assuring clinical equivalence; or

(c) where such validation is not possible, therapeutic equivalence.

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P·M·A

Pharmaceutical Manufacturers
Association
1155 Fifteenth Street, N.W.
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*Copies of the complete report on Drug Bioequivalence may be obtained from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

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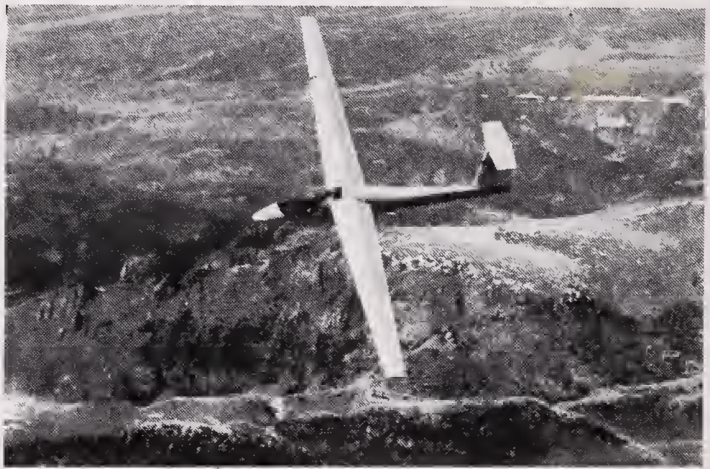

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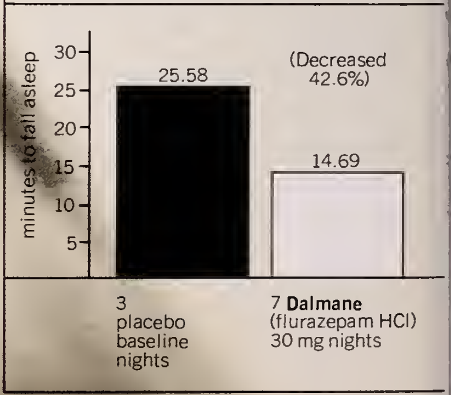

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EFERENCES:

Karacan I, Williams RL, Smith JR: he sleep laboratory in the investigation f sleep and sleep disturbances. Scientific xhibit at the 124th annual meeting of the merican Psychiatric Association, Vashington DC, May 3-7, 1971

. Frost JD Jr: A system for automatially analyzing sleep. Scientific exhibit at he 24th annual Clinical Convention of the merican Medical Association, Boston, Nov 29-Dec 2, 1970; and at the 42nd nnual scientific meeting of the Aerospace ledical Association, Houston, Apr 26-29, 971

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OUR COVER

The August cover honors The Broadmoor where the Colorado Medical Society holds its 105th Annual Meeting. Further details are found on Page 328. Photo credit: Library, Historical Society of Colorado.

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Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

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*Higgs, R. H., Smyth, R. D., and Castell, D. O., Gastric Alkalinization—Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin, *The New Engl. J. of Med.*, 291, 486-490, 1974.

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ON THE FRONTIERS OF DIABETIC RESEARCH...

What is Diabetes?

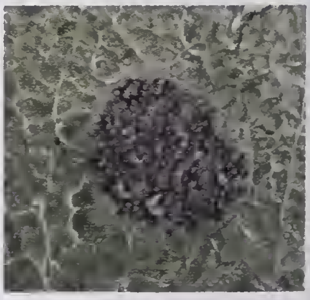
Although a medical scribe of ancient Egypt first made reference to diabetes mellitus in man, today, nearly 4000 years later, only meager specific knowledge exists as to the basic cause of the disease. Without such knowledge it has been possible to provide for limited control only *after* diabetes manifests itself in the form of elevated blood glucose. The possibility of prevention or even cure of diabetes, however, must depend on a full understanding of the genetic defect and/or defects underlying the disease. Our current understanding of diabetes may be compared to our former understanding of another disease of metabolic abnormality, phenylketonuria; only when the genetic lesion of that disease was discovered did it become possible to institute current programs of treatment.

Basic Diabetes Research at Upjohn

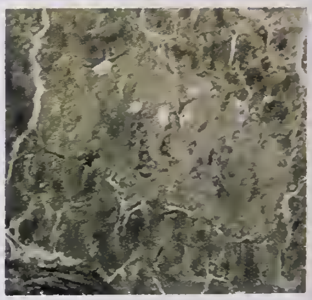
For more than ten years the Diabetes and Atherosclerosis Research Group at The Upjohn Company (W. E. Dulin, Director; G. C. Gerritsen; M. G. Soret; A. Y. Chang) has addressed itself, in a series of unique experiments, to the very basic question: What is diabetes? As with all such fundamental research, practical results are slow in coming and the work of the Group has at times raised more questions than it has been able to answer. It appears now, however, that the research is moving toward important conclusions which may, over the next several years, have significant bearing on our understanding of diabetes and, hopefully, on our ability to control it.

The Chinese Hamsters

In the middle fifties, a group studying cytogenetics in Chinese hamsters at the Children's Hospital Medical Center, Boston, Massachusetts, discovered that certain hamsters develop diabetes spontaneously. The Upjohn Research Group obtained some of these hamsters in 1962, and by controlled inbreeding, succeeded over the years in producing large numbers of diabetic animals for study. To assure continuity of the research in the event of a catastrophe, duplicate breeding stock of all the inbred families are maintained at another site. These are the only such colonies in the United States today. In the course of the research, Upjohn has cooperated with scientists in academic



Normal Chinese hamster, pancreatic tissue. Note blue-stained insulin granules which appear within the beta cells of the islet of Langerhans.



Diabetic Chinese hamster, pancreatic tissue. Insulin granules are almost totally absent. Though beta cells are present, there is some degranulization and vacuolization. The diabetic process is similar to that observed in human pancreatic tissue.

centers, both in America and abroad, in various specialized studies. When possible, these scientists have come to work for a time in Upjohn laboratories. In other cases, specially selected hamsters were transported to outside research facilities.

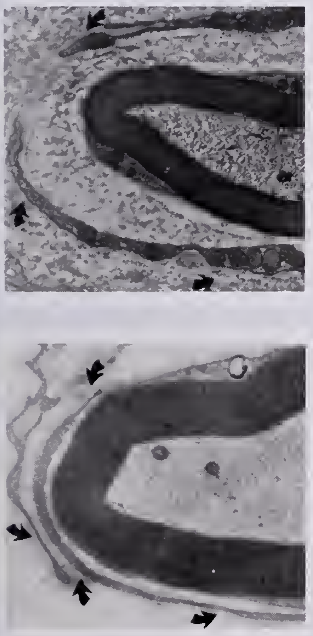
Closer to Man

While other species besides man develop diabetes spontaneously, the Chinese hamster appears to be the best laboratory animal model to study, since its disease is remarkably similar to diabetes in man. Chinese hamster diabetes, like human diabetes, is a complex disease. Like humans, the hamsters have more than one variety of diabetes, including the juvenile, insulin-dependent type as well as the maturity-onset type. They also develop pathological lesions in the retina, kidney, and peripheral nerves, as do human diabetics.

Diabetes is as complicated genetically in hamsters as it is in man. The type and severity of the disease appears to vary with the number of genes involved. Fortunately, genetic analysis can progress faster in the hamster since two or three generations can be produced per year.

Hamsters with Diabetic Genes Overeat

Perhaps one of the most significant observations is that hamsters with diabetic genes have significantly increased food consumption prior to development of clinical signs of diabetes. Further, if the animal with diabetic genes were limited to a normal amount of food, onset of diabetes could be delayed and reduced in severity, and the animal could have a normal life span of 34-35 months. Those animals that develop the clinical symptoms have a shorter life span, which varies with the severity of the disease. Interestingly, decreases in the incidence of human diabetes were noted during the siege of Paris in 1870, and during and immediately after World War II in Europe. It has been postulated that decreased food intake during these periods may have delayed the onset of the disease or reduced its severity to a point where hyperglycemia did not appear.



Peripheral diabetic neuropathy. Top photo, Chinese hamster; bottom photo, 58-year-old diabetic man. The encirclement of myelinated nerve fibers by thin Schwann cell processes, indicated by arrows, is a cellular reaction to chronic demyelination, and is a characteristic finding in this condition in both man and the Chinese hamster.

Implications for the Future

The purpose of the Upjohn Research Group is to attempt, through its work with the Chinese hamsters, to find the basic genetic lesion or lesions associated with diabetes. Such knowledge could provide the information necessary to predict the disease in humans, to define its exact mode of inheritance, and to initiate studies aimed at correcting the defect or defects. Hopefully, it will eventually be possible to devise methods to prevent the development of the abnormalities associated with the disease, if the defect or defects can be corrected. Such methods may replace all treatment in use today.

Already, a beginning has been made in the establishment of programs to apply the information gained from the hamster research. The Upjohn Group is currently working with pediatric endocrinologists in an attempt to define the genetics of human diabetes and to confirm retrospectively whether the discoveries concerning dietary manipulation in genetically diabetic hamsters can be applied to humans. Should the results of these investigations be positive, and if it becomes possible through further work with the hamsters to identify prediabetic humans before they develop signs of the disease, an enormous stride will have been made. Even though the investment in this research is made with no guarantee, this risk must be undertaken.

Note: For bibliography of published papers, please write to W. E. Dulin, PhD, Upjohn Diabetes and Atherosclerosis Research Group, 7241-25-9, Kalamazoo, Michigan 49001.

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2. Method of preparation. All material for publication must be typewritten, double spaced, with liberal margins, using only one side of the paper, pages consecutively numbered, and preferably on standard 8½ x 11 white bond paper. Carbon copies are *not* acceptable.

Title (preferably short) and author's name, city and state must appear at the top of the first page. Second and subsequent pages should be identified with consecutive page numbers and author's surname. If physician authors possess more than one degree, the MD only is used. Lesser degrees of non-MD authors or co-authors may be used.

Please include beneath the title or at the top of the first page a brief paragraph stating what the article is designed to show and, therefore, why it should be read. This introductory feature is, in editorial parlance, called the "blurb"; it is printed in bold type.

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12. Editorials. We would like to have more submitted by our State editors and the membership at large. Readers must get tired of thunder from publication headquarters in Denver; frankly, we do too! Speak out, and we'll sign your name, initials, or respect your request for anonymity, as you choose. If you don't like something we do or say, please let us in on it; we could even stand to hear about it if something happens to please you. A "Letter to the Editor" may help you get something off your mind. We're asking for it and we have a place to put it—in the Journal, that is!

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Changing Role of the Voluntary Health Agency

Long-term planning is appropriate both for public and private agencies. Unfortunately, because of politics and our triparite system of government, long-term planning is sometimes sacrificed for political gains. A review of long-term goals for voluntary health organizations is the purpose of this short communication. There will be decreased need for support of health services by philanthropy. Particularly in hospital care, because of government takeover of this activity there will be little need for voluntary agencies. In other words, hospital care will be provided by government subsidies and heavily regulated private insurance companies, and one can expect private philanthropy and voluntary health agencies to back off from support of this type of health activity.

On the other hand, provision of "venture capital" for new services, especially outpatient activities, will be a major sphere of voluntary agencies because government will not be able to do this. Government will be handicapped by the increased tremendous demand for pure services and by constant deficit spending for just plain services. The areas in which private agencies will be able to do better than government include the following: a) experimentation, b) updating standards of medical care, c) research in unrecognized fields and the recognized fields, d) new methods of treatment, education and research, and e) certain outpatient treatment such as special clinics. Government agencies will be encouraged by private agencies to appoint commissions and special study groups, probably from members of the private agencies. However, the real capital will probably come from the private factor. The private agency input on these special commissions and study groups will target on select national and regional priorities.

"Consumerism" will be a definite sphere of activity for the private health agency. The shifting of financing of medical care to the federal level will ignore unmet local needs, in particular, in two areas: a) minority groups whose voices may not be heard, b) assessment of the performance of the public agencies. In other words, a "watchdog" type of function would be ideally supported by private agencies, many of whom in turn are supported by minority groups and patients with "the disease" (multiple sclerosis, cancer, heart disease, etc.).

In summary, private health agencies will have plenty to do in the future. 1) They will be the financial support for new ways of doing things, assessment of standards of medical care in the teaching institutions, selection of research projects which may not be afforded by the public groups, support of research in unrecognized fields, new methods of treating disease, experimentation. 2) They will provide consumerism in which the public programs are watched over by the voluntary and private health agencies. Cooperation between the two groups will not only be helpful, but earnestly sought by both.

Charles D. Magill, MD, Englewood*

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* Dr. Magill was formerly President of the Tri-County District Board of Health, and is President of the Central Colorado Chapter of the National Multiple Sclerosis Society.

THE HOUSE OF DELEGATES of the AMA has decided to take the bull by the horns. There is no logical option. Admit the mistakes — reorganize and streamline — reemphasize the goals — press the attack. This means raise the dues.

AMA ON THE ATTACK

Obviously the major mistake over the past five years was acceptance by the House and the Board of deficit budgets, which depleted the financial reserves of the Association. Also, there was the insidious and inevitable growth of the bureaucracies of the organization and laxity in their financial monitoring. Finally, the potential of the changing economy was not appreciated. However, actually even the financial reserves could not have covered for long the soaring costs of operation due to inflation.

On the other hand, especially in the legislative area, there have been major achievements, of which many seem unaware. Last year on threat of suit by the AMA, the Secretary of HEW withdrew the proposed requirement of utilization review for preadmission certification. A suit against HEW contesting the validity of utilization review regulations continues to postpone the effective date of compliance with these regulations. A lawsuit supported by AMA research and legal aid against a hospital board of trustees who tried to unilaterally rescind the by-laws of the medical staff was won by the staff. AMA is now challenging in court proposed government regulations to set maximum allowable cost of drugs (MAC) for patients in federal health programs. Likewise, the AMA plans by lawsuit to challenge the Health Planning and Resource Development Act, the most threatening and powerful federal health bundle which the congress has ever passed. AMA is committed without restrictions to take whatever legal steps are necessary to solve the professional liability problem.

But the push by the liberals for socialized medicine is relentless. Our only effective antagonist at the federal level and in the halls of Congress is the AMA. A congressional lobby is expensive. The costs required to challenge in the courts federal health laws and directives of federal bureaus is unbelievable. The political approach through AMPAC, financially independent of AMA, of course helps to elect candidates who support our philosophies of medical practice, but the day to day battle against government control must be waged by the AMA. The source of the funds must be the dues dollar.

The raise in AMA dues is substantial. How many members will be lost? Some. Times are hard, business is down, and the physician faces rising expenses of inflation and disgraceful soaring costs of liability insurance. There are competing financial demands for support of local wars. The House was aware of these problems. But, the great majority of physicians still do not plan to surrender without a fight. The bulk of the profession is going to try to stop the liberals from destroying private enterprise in medicine, saddling Americans with inferior health care, and bankrupting the nation. In this bicentennial year, when we are remembering what it meant to be a colonist in rebellion, a famous quote of a forebear is appropriate to this discussion. When asked by the enemy, because his flagship was sinking, if he were surrendering, John Paul Jones replied, "I have not yet begun to fight."

More On Our Cover

Count James de Pourtales who developed the Broadmoor Casino in 1891 hoped it would outshine Monte Carlo. He had come to America from Silesia, Germany to increase his fortune. First he bought an interest in the Willcox Dairy, which he planned to make a major American herd.

He then built a lake, then the Casino facing it. He was able to persuade the Colorado Springs Company to extend trolley service from Colorado Springs, and visitors started coming out to look the Casino over. The number of curious fell when silver dropped out of sight, and there were those who felt this was a natural retribution for anyone encouraging gambling in their midst. In 1897 the Casino burned down.

Forthwith, Pourtales turned to Arizona mining interests in association with Richard Penrose, a Pennsylvanian come West to build a fortune. This time Pourtales was successful, and presently earned enough to retire to Silesia. Ultimately it was Spencer Penrose, younger brother of Richard Penrose, who implemented the Pourtales dream of a great hotel at the Broadmoor.

Over a great many years the Colorado Springs area has been a popular location for CMS Annual Meetings, more than thirty having occurred there. The first Colorado Springs area meeting took place in 1879, when 64 members were in attendance. Since 1964, CMS has held 11 annual meetings at The Broadmoor.

Comprehensive treatment of childhood muscular dystrophy*

Fred A. Ziter, MD and Kent G. Allsop, RPT, PhD,
Salt Lake City

Duchenne Muscular Dystrophy (DMD) has the following characteristics: (1) onset between three and six years of age; (2) moderately rapidly progressive muscle weakness, wasting and contractures, affecting the lower and then the upper extremities; (3) relative sparing of cranial nerve muscles; (4) loss of ambulation and confinement by 8-12 years; and (5) more slowly progressive generalized weakness in the teen years, leading to respiratory failure before the third decade. The disorder is inherited as an x-linked recessive trait. Usually only males are affected, whereas females who are clinically normal are carriers. The nature of the fundamental biochemical defect is unknown in spite of research efforts spanning decades. DMD is the most frequent and disabling of the childhood neuromuscular disorders.

The long list of drugs unsuccessful in modifying the course of DMD is disheartening. Authorative reviews focus mainly on theories of its pathogenesis and clinical nuances of the disease but convey hopelessness when discussing treatment.[1,2] The practitioner may feel understandably helpless, patient and family despair is almost unavoidable, and the attitude of "keep the child happy" becomes the foundation of therapy.

The purpose of this paper is to outline a positive therapeutic approach to DMD. The approach is based on two premises: (1) there are predictable and preventable secondary factors which magnify significantly the weakness and wasting; (2) an active program of physical therapy, medical monitoring and family support will enhance the qualify of life of these children. The approach we describe has been reported by others[3] but is modified by our experience in the Muscle Clinic at the University Hospital. The principles described are directed toward patients with childhood muscular dystrophy, but many also apply to other forms of neuromuscular disease.

A description of various modes of presentation and diagnosis will precede the section on treatment. The need for accuracy of diagnosis is evident, since the implications are far reaching.

Diagnosis

Patients with DMD will be seen by the physician under three clinical circumstances depending on age:

Infant to Three Year Old: Patients in this group are usually asymptomatic but parents request evaluation because of a history of DMD in maternal family members. Occasionally the clinical examination shows minor abnormalities, but it is seldom conclusive. In such cases laboratory studies prove invaluable. The serum creatine kinase (CPK) is markedly elevated in the preclinical dystrophic. This test is virtually diagnostic of the disorder in the presence of a positive family history in spite of a lack of clinical weakness. Muscle biopsy will show the characteristic changes of fiber size variability and necrosis. The electromyogram (EMG) reveals small motor units, but interpretation in the very young is difficult.

Three to Six Year Old: In this age period patients with DMD begin to show evidence of clinical weakness. Repeated falling and toe walking are common complaints. Muscle weakness is manifested by waddling, particularly when running, and slight difficulty

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[1] From the Department of Neurology, College of Medicine and College of Health, University of Utah, Salt Lake City. This work was supported in part by a grant from the Muscular Dystrophy Associations of America.

standing after being seated on the floor. Pseudohypertrophy of the calves is noted, and palpation of pectoral girdle muscles reveals early wasting. The knee jerk is depressed or absent.

Because clinical muscle testing is difficult if the child is uncooperative, the clinician must use the serum CPK level, EMG and muscle biopsy to establish the diagnosis. Serum CPK will be elevated to levels 25 to 50 times the normal range in patients with DMD, and lack of such elevation should raise doubts about the diagnosis. Muscle biopsy and electromyography are mandatory if the diagnosis is in question. We perform these studies for final corroboration on all patients with DMD.

Six and Older: Presentation in this age group has the advantage of relative ease of diagnosis. Most patients show characteristic weakness of both upper and lower extremities, muscle wasting and demonstrable gait abnormalities. Muscle involvement is generalized but particularly prominent in the pectoralis, lower trapezius, latissimus dorsi, biceps and brachioradialis in the upper extremities and the gluteus maximus, quadriceps, peronei and tibialis anterior in the lower extremities. This relative selectivity is a mystery,[4] and its explanation may someday provide a clue to etiology. The weakness of lower extremity muscles leads to a characteristic gait in dystrophics of this age. The gait is wide based and waddling particularly when the patient runs a short distance. When he rises from a sitting position on the floor the patient exhibits a characteristic "climbing up himself" (Gower's sign), a vivid display of proximal lower extremity weakness. Exaggerated lumbar lordosis, calf pseudohypertrophy, abdominal protuberance and a tendency to toe-walk are also characteristic.

Treatment

After the diagnosis of DMD has been established, one should counsel the parents and patient. This may be time consuming but is essential for an effective program. Some of the discussion dealing with genetic counseling, anticipated disability and ultimate prognosis should not include the patient. Those aspects dealing with symptoms, treatment and the establishment of realistic goals for the patient and parents should be openly discussed and reinforced repeatedly. A positive approach is crucial because the disorder has a chronic progressive course with great impact on the family and an unalterably fatal outcome. Our treatment program is based on hope of success, albeit limited, which must be continuously reappraised and reinforced in the patient and family.

Since the muscle degeneration cannot be prevented with a specific treatment, the program aims to prevent or eliminate commonly encountered secondary factors which contribute significantly to disability, hasten the muscle wasting and precipitate premature loss of ambulation. These factors include: contractures, disuse atrophy, obesity, medical complications and various emotional factors.

Preventable Disability

Early in the course of DMD preferential weakness of gluteus maximus, quadriceps and anterior tibial muscles leads to compensatory postures such as exaggerated lumbar lordosis and toe-walking. Such postures reflect the patient's involuntary compensatory effort to remain erect by realigning the center of gravity. Flexion contractures of the hips, knees and ankles result from the muscle imbalance and are predictable and often exaggerate the disability. They can be prevented by range of motion exercises performed by the parents at home, carefully monitored by the physical therapist at the time of periodic clinic visits. The parents are instructed to perform these simple exercises for about ten minutes twice each day, and the patient is instructed to assist actively in the maneuvers. We have found it more beneficial to institute the home program early and prevent the contractures, rather than delay treatment until they appear.

There are many disadvantages when diagnosis has been delayed until this degree of progression. Parents are frustrated because an explanation of their child's problem has not been rendered. The lack of genetic counseling may have resulted in the generation of younger siblings susceptible to unanticipated disease. The process of acceptance of the diagnosis, understanding the prognosis and the plan for treatment require time. Finally, those who have worked with these children recognize that early treatment results in better psychologic adjustment by the patient and significantly postpones the dependent status of the wheelchair-bound dystrophic.[3]

Active exercise should be encouraged, but over exertion may cause falling and should be avoided. Although some programs stress a routine active exercise program,[3] we believe that ambulation sufficient to satisfy the child's home, school and recreational needs provides a more useful program. Prolonged periods of inactivity at home and in school should be avoided.

The degree of supervision required to conduct the home program properly varies, but we find that assessment is required by the therapist every three months. Clinic visits spaced at longer intervals result in less control of contractures, because the interest of patient and family declines.

Contractures in the upper extremities follow the muscle wasting more closely and are less amenable to treatment than those in the legs, but they produce less functional disability. However, we do encourage elbow extension, forearm supination and wrist extension maneuvers.

Prolonged inactivity has a detrimental effect on muscle strength in the child with DMD. Many authors have recounted cases of ambulatory dystrophics, confined to bed for illnesses who were never able to resume walking. This has led to the philosophy that bed rest beyond several days requires extra effort to maintain muscle strength while the patient is confined. Early postoperative ambulation is essential after elective procedures, and light-weight walking casts must be employed early in the treatment of fractures of the lower extremities. The physician should be notified if the child is confined to bed, so that provisions may be made for increased therapy at home.

Since inactivity can be detrimental, we even discourage continuous inactivity beyond periods of one or two hours aside from sleep. Sitting in front of a television set with the lower extremities flexed should be discouraged, whereas lying in the prone position will lessen hip flexion contractures. The child should be encouraged in activities which can be performed while standing. A general goal of at least three hours of standing or ambulation each day is realistic and adequate to maintain strength and discourage the development of contractures. The child who has regressed to less than this amount of ambulatory time will likely lose unassisted walking within several months. We avoid the use of a wheelchair in ambulatory patients because they quickly become dependent upon it, particularly when it is encouraged by well-meaning relatives and schoolmates. In busy school corridors the child with a precarious gait can be allowed to leave class early to proceed to his destination unjostled. A wheelchair is allowed only when prolonged ambulation would be unduly fatiguing or risky.

Braces and Surgical Procedures

Use of braces and surgical procedures in order to prolong ambulation in patients with DMD has been controversial.[7] Some authors hold that the rewards of bracing do not warrant the expenditure of energy required by the patient and family. We, like many others, do not adhere to this philosophy. Long leg braces can extend significantly the period of ambulation and, when successfully employed, have a positive emotional effect. Braces also delay the development of contractures and disuse atrophy. The proper time to initiate braced ambulation is critical. Long leg braces tend to impede ambulation, when they are applied prematurely, but will satisfy a real need when their use is withheld until independent walking is about to cease. Vignos[3] has found that approximately one year after the inability to climb stairs, or six months after the inability to arise from a chair, the patient will lose ambulation. A further guide to imminent loss of ambulation is decrease in daily ambulation time to less than one hour and the need for external support while walking. Successful braced ambulation is still feasible, but far more difficult, if the child has been confined to a wheelchair for several weeks or months.

Several types of orthopedic procedures have been used to improve ambulation including heel cord lengthening, iliotibial band fasciotomy and posterior tibial tendon transfer. Toe walking in the ambulatory dystrophic should be recognized as a compensatory mechanism necessary for knee joint stability. The resultant heel cord contractures are common. A tenotomy performed in the period of independent ambulation will cause recurrent contractures, or the patient ceases walking because of gastrocnemius weakness. We advise heel cord lengthening only at the time long leg braces are applied, if the home program has not been sufficient to prevent contractures. Iliotibial band fasciotomy (Yount) has been recommended by some, but we have not found it necessary. Posterior tibial tendon transfer has been advised for equinovarus deformity which interferes with ambulation. We have not used this procedure, since the varus deformity can be avoided with a good home program and neutralized by the ankle support of long leg braces.

The inactivity of permanent wheelchair confinement leads inevitably to progressively deforming contractures, but these can be minimized by continued physical therapy and certain postural adjustments. Lying in the prone position will reduce hip flexion contractures, and elevation of the leg rests on the wheelchair will retard knee flexion deformities. Surgical correction of foot deformities is not recommended for the non-ambulatory dystrophic.

Obesity: There are several factors which predispose the patient with DMD to obesity. These are inactivity, boredom and overfeeding by family and friends. Many authors think obesity is one of the major factors causing premature loss of ambulation. We believe obesity impairs all phases of treatment. The hazards of obesity in patients with weakness are explained to the patient and family during initial visits. Prevention of obesity is simpler than weight reduction and is another reason to stress the subject early. It may be necessary to alter the entire family's diet to prevent or treat the problem.

Medical Complications

The complications peculiar to patients with DMD are due to the effects of muscle degeneration. During the late ambulatory period patients are particularly liable to injury, especially fractures of the thinned bones of the extremities. The fracture problem is serious, since prolonged immobilization often results in permanent loss of ambulation. Recognition of this has prompted early ambulation and light-weight walking casts with moderate success. The dangers of bed confinement during medical illness are similar.

The ambulatory dystrophic tolerates the usual childhood diseases reasonably well. Routine immunizations should be given and no unusual precautionary methods, such as influenza vaccinations, are necessary. The risk of life threatening pneumonia increases as weakness progresses and in advanced cases is the major cause of death. The key abnormality of pulmonary function in DMD is restricted respiration and reduced vital capacity. The primary cause is respiratory muscle weakness, but scoliosis, elevated (dystrophic) diaphragms, atelectasis and pulmonary fibrosis are contributing factors. In advanced dystrophics upper respiratory infections may lead to bronchial involvement and the symptoms of dyspnea, cough and fever. Aggressive respiratory care in the hospital, which provides close monitoring, appropriate antibiotics, postural drainage and intermittent positive pressure breathing should be provided. The use of chronic assisted ventilation should be avoided.

Cardiomyopathy is present in virtually all patients with DMD.[5] Tachycardia and distinctive electrocardiographic changes are noted during the first decade. Congestive cardiac failure and arrhythmias are described but they are not encountered frequently. Perhaps the restricted physical activity imposed by muscle weakness has a saving effect on compromised cardiac function.

The risks of anesthesia increase as weakness progresses. The respiratory depressant effect of barbiturates, cardiotoxic properties of halothane, and deleterious effect of standard doses of succinylcholine should be avoided. Careful attention by the anesthesiologist to cardiac monitoring, adequate ventilation, avoidance of potassium overload and gastric dilatation are important.

Emotional Factors

Although a small per cent of patients show high intellectual achievement, strong motivation and excellent emotional adjustment to their disease, many with DMD have emotional disturbances. Many patients show passitivity, restricted interests, withdrawal and emotional immaturity. They also have very limited motivation, accept setbacks willingly, and passively resist outside efforts to promote their improvement.[6] These emotional characteristics have been ascribed to several factors. Their muscle weakness and limited physical capability obviously restrict their environment and place them in an increasingly dependent position. Mild to moderate restriction of intellect common in these children further lowers their educational achievement and ability to cope with their disease. These young patients are especially vulnerable to intrafamily tension since there is virtually total reliance on parents. Finally, there are undoubtedly complex psychologic adjustments when a child realizes he has a poorly understood, debilitating disease which will erode his life to the point of mere existence and then, perhaps as a relief, produce premature demise.

The emotional problems are common and must be managed with vigor if the program is to be successful. We focus our treatment on the entire family, since they are all influenced by the disease. This approach is more satisfactory, since the patient's ability to cope with these problems is limited. By offering support frequently and reinforcing the goals of treatment, the average family is capable of resolving many of the emotional problems. A skilled social worker can be invaluable when one encounters more resistant cases, and occasionally psychiatric consultation is needed.

Effectiveness of Treatment

All do not agree with the treatment program we have described. Many competent physicians will permit the early use of a wheelchair to avoid trauma and undue physical hardship for the family. Many believe that braced ambulation is not justified, since it requires a large commitment by the patient and family and only postpones the time until the child can "relax" in his wheelchair. This approach is not unreasonable and is all that can be accomplished in some cases.

However, if one employs an active home program, unassisted ambulation can be prolonged about one year. Bracing will allow continued ambulation for approximately two more years. Braced ambulation with assistance and braced standing will postpone the wheelchair further for one to two more years. The overall program under ideal, but not unrealistic, circumstances will result in greater independence for at least four years.[3] There are no data to suggest that longevity is extended with this approach, but carefully controlled studies have not been reported.

We believe this approach offers more than any other, in the absence of a specific treatment for the underlying disease. We also recognize that if a specific treatment does become available, those patients in optimal physical condition will reap the greatest benefits.

Summary

Duchenne muscular dystrophy is almost as poorly understood now as it was when first described more than a century ago. Although much research is being done, the primary metabolic defect remains elusive, and a specific treatment has not been found. We have outlined a comprehensive treatment program specifically designed to deal with the secondary complications which often overshadow the primary muscle degeneration and contribute significantly to overall disability. Although the approach which has been outlined is controversial, we believe the overall benefit of more prolonged ambulation allows greater independence and an enhanced quality of life. •

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Acute Promyelocytic Leukemia*

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In 1957 Hillstadt published the first description in English of a peculiar type of leukemia characterized by predominance of promyelocytes, severe bleeding tendency, and rapid clinical deterioration.[1] He found several possible earlier cases of this entity in the English literature which he termed Acute Promyelocytic Leukemia (APL). Several descriptions of this same entity appeared in the French literature in the late 1940's and early 1950's with a description by Croizat and Favre-Gilly appearing in 1949.[2]

Since these early reports, the disease has been better defined. Its major characteristics include a profound bleeding tendency, the absence of organomegaly, a predominance of promyelocytes, and early death. Initial reports attributed the bleeding tendency to excessive fibrinolysis. More recently it has become apparent that disseminated intravascular coagulation (DIC) is the cause of the hemorrhagic tendency, and that concept is supported by evidence that material from the malignant promyelocyte is procoagulant, and the cause of DIC.[3] Electron micrographs of promyelocytes from APL are reported to show a characteristic morphology, different from that of normal promyelocytes.[4]

APL is not reported with equal frequency from different parts of the world or even by different centers within this country. The generation of accepted minimal diagnostic criteria for APL may alleviate some of the confusion in the literature about the diagnosis of non-lymphoblastic acute leukemias. Until recently APL had a worse prognosis than the other acute non-lymphoblastic leukemias. However, beginning with some reports of treatment with Daunorubicin, and then combining aggressive antileukemic therapy with treatment of the accompanying DIC, some therapeutic success has been noted. The entity now seems to be at least as responsive to treatment as other acute non-lymphoblastic leukemias. The purpose of this paper is to discuss a patient with APL and DIC who responded to heparin and chemotherapy, and to review the recorded cases of acute promyelocytic leukemia to better define the disease, its response to various types of treatment, and prognosis.

CASE REPORT

A 49-year-old farmer first noted moderate fatigability and bleeding from his gums early in 1972. In March 1972, four teeth were removed for caries, and following their extraction the patient had uncontrolled bleeding. Suturing of the extraction sites was ineffectual. The patient was given packed red blood cells, and platelet transfusions. On March 25 he was referred to the University of Nebraska Medical Center after a bone marrow disclosed evidence of hematologic malignancy. Prior to the onset of the present illness, the patient had been in good health.

Physical examination disclosed the presence of periorbital hematomas, and bleeding from the extraction sites in the maxillary area. Blood filled the entire oral cavity. The patient's initial hemoglobin was 10.4 gms%, his white blood count was 2,500 with 38% progranulocytes, 33% blast cells, 11% segmented neutrophils, 8% bands, 9% lymphocytes, and 1% eosinophils. There were 7 nucleated red cells per 100 white cells. The platelet count was 25,000 and the reticulocyte count 5.1%. A bone marrow showed increase of total cellularity with a predominance of progranulocytes, diminished numbers of normal granulocyte precursors, and megakaryocytes. Additional laboratory studies showed LDH of 854, a fasting blood sugar of 270 mg%, an unremarkable protein electrophoresis, fibrinogen degradation products (FDP) of 205 mcg/ml, a positive ethanol gel, plasma protamine paracoagulation and serial dilution protamine sulfate tests. The euglobulin clot lysis was greater than 2 hours; prothrombin time was 13 seconds with a control of 11. The partial thromboplastin time was 33/43 and the thrombin time 18/13. Specific factor assays are shown in Table 1. Admission fibrinogen was 120 mgs%.

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* From the Division of Hematology and Department of Internal Medicine, University of Nebraska Medical Center, Omaha, Nebraska.

TABLE 1

Serial Coagulation Values* in Patient W.C. (Normal Values Indicated in Parentheses)

Date	Prothrombin Time (sec)	Partial Thromboplastin Time (sec)	Thrombin Time (sec)	Fibrinogen Titer	Ethanol Gel	SDPS	FDP ug/ml	Coagulation Factors
3-25	13 (11)	33 (43)	18 (14)	1:81 (≥1:81)	Pos (Neg)	Pos (1:40)	205 (6)	II:70% (60-130); V:50% (70-125); VIII:40% (60-180); IX:150% (60-160); XI:140% (60-150); XII:110% (60-150)
3-27	12	36	14	1:81	Neg	Neg	147	
3-30	12	39	18	1:81	Pos	---	121	
4-4	11	32	13	1:243	Neg	Neg	60	
4-5	11	32	15	1:243	Neg	Neg	0	II:100%; V:100%; VIII:130%; IX:110%; XI:140%; XII:110%
4-13	11	31	14	1:243	Neg	Neg	563	
4-14	12	29	13	1:243	Neg	Neg	2	
6-29	10	36	13	1:243	Neg	Neg	5	
10-30	15	47	22	1:27	Pos	Pos (1:40)	74	
11-6	14	41	20	1:81	Pos	Pos (1:40)	74	

* Certain coagulation studies were performed as reported previously.[50] Determination of FDP was done according to the method of Hawiger et al.[51], SDPS by the method of Gurewich[52], ethanol gel by the method of Breen and Tullis[53], fibrinogen titer by the method of Hardisty[54], prothrombin by the method of Denson[55], and factors IX, XI and XII by one stage assays using specific deficient substrate plasma.[54]

The patient was treated with 6-Mercaptopurine 50 mgs. twice daily, allopurinol 100 mgs. tid. and cytosar 100 mgs. intravenously daily for 5 days. Heparin was begun, at 4,000 Units every 4 hours. Regular and NPH insulin also was given (60 to 100 Units/day). The patient was febrile with a temperature of 104°F on admission and blood cultures grew alpha hemolytic streptococci. He was treated with Keflin intravenously. The problem of intraoral hemorrhage was partly controlled by the use of packing, and bleeding gradually subsided. The patient was discharged on the 7th of April, free of bleeding and taking 6-Mercaptopurine.

Six days after discharge he was readmitted because of fever without chills, sweating or localizing symptoms. His temperature on admission was 100°. Examination disclosed a moderate number of petechiae and ecchymoses at the injection sites, where he had received insulin. There was no organomegaly. Admission hemoglobin was 9.1 gms%; the white blood count was 1,000 with 16% segmented neutrophils, 60% lymphocytes, 4% eosinophils, 20% progranulocytes and 2 nucleated red cells/high powered field. The platelet count was 6,000. Reticulocyte count was 0.8%. FDP were 563 mcg/ml, the fibrinogen 550 mgs%. Prothrombin time was 11 sec. (control of 11). The partial thromboplastin time was 31 sec. with a control of 45 secs. Blood cultures grew pseudomonas aeruginosa, and accordingly the patient was treated with carbenicillin and gentamycin intravenously. A repeat bone marrow was done which showed hypercellularity with abundant numbers of promyelocytes, and the patient was given a second course of cytosine arabinoside and 6-Mercaptopurine. Heparin was given, and after one day the patient's FDP were noted to be 2 ug/ml (Table 1). The patient was discharged on April 29, the 17th hospital day on 6-Mercaptopurine maintenance.

When seen as an outpatient on May 10, the white count was 3,300, his hemoglobin 12.3 gms, his platelet count was 630,000 and reticulocytes were 1.4%. He was maintained on 100 mgs. of 6-MP daily and followed through the summer of 1972, at which time his white counts ranged between 5,000 and 7,000. His hemoglobin remained normal, the platelets were 200-400,000/cu mm. and his reticulocytes were 2-4%. During that time the peripheral blood differentials were unremarkable.

In July 1972, his peripheral blood showed no abnormalities, and it was elected to extract six carious teeth. The patient did not have a significant degree of blood loss, and was discharged on the 3rd hospital day.

The patient was readmitted on the 30th of October with a white blood count of 2,900, a platelet count of 29,000 and a hemoglobin of 16.4. The peripheral differential showed 58% segmented neutrophils, 5% bands, 22% lymphocytes, 10% monocytes, and 2% eosinophils. Two progranulocytes and 1 myelocyte were noted on the peripheral smear. He was essentially asymptomatic. Physical examination was unremarkable. The ethanol gel test was positive. The plasma protamine paracoagulation and serial dilution protamine sulfate were positive, the thrombin time was 22 seconds with a control of 13 and the FDP 74 ug/ml. The patient accordingly was given 2,000 Units of heparin every 6 hours. A bone marrow showed hypercellularity with more than 40% of the cells being promyelocytes. Cytosar 100 mgs. intravenously was begun and 6-MP 150 mgs/day was continued. On the 2nd hospital day heparin was increased to 3,000 Units every 4 hours. The patient's platelet count and white blood count continued to fall with the platelets being measured at 6,000 on the 5th hospital day and the peripheral white count being 2,700 with 53% segmented neutrophils, 10% blasts, 10% progranulocytes and 3% myelocytes. The ethanol gel, 3P and SDPS were positive on November 6, the day of death.

Autopsy showed subarachnoid and intracerebral hemmorhage, which was multifocal but dissected along the external capsule and into the left frontal lobe. There were also multiple localized foci of cerebral hemorrhage. The spleen weighed 620 gms. Microscopic sections of the spleen showed the architecture to be distorted and congested, with scattered leukemic infiltrates present in the parenchyma. Focal pulmonary edema also was noted.

Discussion

At least 214 cases of APL (avoiding duplicates) have been reported in the literature to date.[1,2,4,6-43] The incidence within various

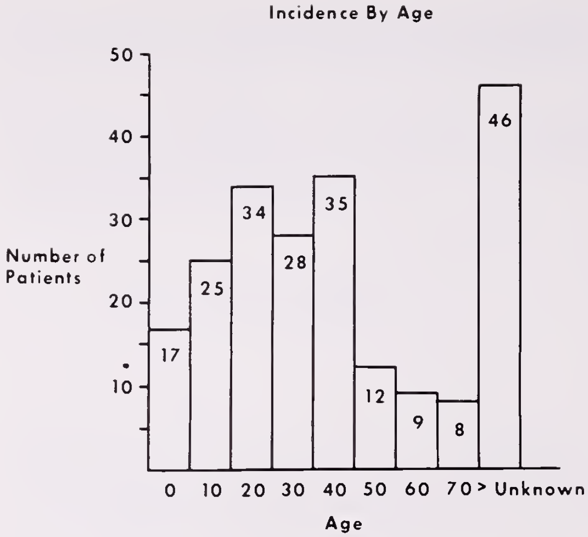

Fig. 1. Occurrence of Acute Promyelocytic Leukemia by Age.

TABLE 2
Results of Initial Coagulation Studies in Patients with Acute Promyelocytic Leukemia

Test	Results - Number of Cases (%)	
	Normal	Abnormal
Bleeding Time	0 (0%)	13 (100%)
Platelet Count	4 (3%)	149 (97%)
Fibrinogen	18 (19%)	75 (81%)
Prothrombin Time	10 (20%)	39 (80%)
Partial Thromboplastin Time	8 (73%)	3 (27%)
Thrombin Time	1 (8%)	12 (92%)
Fibrinogen Degrad. Prod.	4 (17%)	20 (83%)
Clotting Time	12 (63%)	7 (37%)
Clot Lysis	10 (40%)	15 (60%)
Prothrombin-Proconvertin	1 (20%)	4 (80%)
Coagulation Factors		
II	15 (88%)	2 (12%)
V	13 (42%)	18 (58%)
VII	3 (75%)	1 (25%)
VIII	7 (70%)	3 (30%)
IX	7 (100%)	0 (0%)
X	2 (67%)	1 (33%)
VII & X	15 (68%)	7 (32%)

series of acute leukemia has varied from non inclusion of APL[5] to approximately 12 per cent.[1] In the largest series of APL yet published (Bernard et al),[41] the incidence was 5 per cent of all acute leukemias. While the disease is uncommon, it is not rare and probably will be seen regularly by all centers treating acute leukemia.

APL has been reported in patients with ages ranging from 3 to 82. (Fig. 1). While the disease has been most commonly reported in young adults, there is no predilection for any age. This differs from acute granulocytic leukemia, in which children are much less commonly affected and the disease is most prevalent in older age groups.[44] Sex differences in acute promyelocytic leukemia are absent, with 49 per cent of reported cases being male and 51 per cent female. In contrast, acute granulocytic leukemia has a distinct male predominance.[44]

Clinical manifestations of acute leukemia are related either to an absence of normal hematopoietic cells (e.g. dyspnea, related to anemia), or the presence of a malignant cells disrupting normal organ function (e.g. CNS leukemia secondary to invasion by leukemic blasts). In acute granulocytic leukemia, symptoms are generally related to the absence of normal hematopoietic tissue, and include infections, petechiae or other bleeding related to thrombocytopenia. It is unusual to have symptoms directly related to the presence of the myeloblasts. APL may be associated with similar symptoms. However, these are often overshadowed by the hemorrhagic diathesis presumably related to the particular type of malignant cell proliferation.[3] In the 89 cases in the literature in which the presenting symptoms are recorded, 97 per cent presented with hemorrhagic manifestations. In acute granulocytic leukemia only 54 per cent of patients are found to have manifestations of hemorrhage at presentation,[44] and only 8 per cent of patients seek medical attention because of bleeding. In APL, however, hemorrhage is the most common presenting complaint. Bleeding in APL most commonly has been purpura, but also reported are hematuria, vaginal bleeding, rectal bleeding, bleeding from gums and nose, hemorrhage in the joints or eyes, hemoptysis, and "generalized bleeding." Most patients will also demonstrate pallor and many will show signs of infection. Of the reported cases of APL, 26 per cent had palpable hepatomegaly, 19 per cent had palpable lymphadenopathy, and 21 per cent had palpable splenomegaly. In contrast, acute granulocytic leukemia is associated with hepatomegaly in 54 per cent of the patients, lymphadenopathy in 47 per cent and splenomegaly in 60 per cent.[44] The absence of hepatomegaly, lymphadenopathy, and splenomegaly at the time of diagnosis is one of the hallmarks of acute promyelocytic leukemia.

Laboratory abnormalities in APL include a white count of less than 5,000 (50%) while only 24 per cent had a white count of greater than 10,000. In contrast, 27 per cent of the patients in other types of acute leukemia had white counts

TABLE 3

Contrasting Findings in Acute Promyelocytic Leukemia and Acute Granulocytic Leukemia

	APL	vs	AGL
Age	All ages--most cases young adults		Uncommon in children, most common in older age groups
Sex	No difference in incidence		Striking male predominance
Symptoms	Related to Hemorrhage in 97%		Related to Hemorrhage in 54%
Physical Findings			
1. Enlarged Liver	26%		54%
2. Enlarged Lymph Nodes	19%		47%
3. Enlarged Spleen	21%		60%
Laboratory Abnormalities			
1. Leukopenia	52%		27%
2. Abnormal Promyelocyte	present		absent
3. DIC	present		uncommon
Cause of Death	Hemorrhage 79%		Infection >50%

less than 5,000 at diagnosis and the majority demonstrated leukocytosis.[44]

The most specific finding for the diagnosis of acute promyelocytic leukemia is the presence of abnormal promyelocytes. This cell has been well described in the literature and is characterized by a large number of very prominent, dark staining granules and often the presence of multiple Auer rods with a unique morphology.[45] These cells were seen in the peripheral blood in 87 per cent of the reported cases of APL and comprised more than 50 per cent of the cells seen in the peripheral blood differential in 31 per cent. The atypical promyelocyte accounted for greater than 50 per cent of the cells seen in the bone marrow in 93 per cent of the reported cases.

When examined in the electron microscope the promyelocyte of APL is said to show distinctive nuclear indentation, granules 400 to 800 mμ in diameter, occasional well-developed tubular formations, numerous large mitochondria, occasional Auer rods, well-developed rough endoplastic reticulum and Golgi apparatus, and an unusual fibrin-like structure in the rough surfaced endoplasmic reticulum.[4] Recent publications have supported the concept of morphologically unique hypergranular cells which bear a causal relation to the occurrence of DIC.[40,46] These cells often have faggots of Auer rods and/or heavy granules, in distinction to the granulation of myelomonocytic leukemic cells.[46] Cells with heavy granulation may have the potential to activate coagulation by activating factor X,[3] and have tissue factor activity as well.[3]

Eighty-seven per cent of patients with APL were anemic (hemoglobin less than 12 grams) at the time of diagnosis, and one-half of the patients had a hemoglobin of less than 8 grams. These values are similar to those previously reported for other types of acute leukemia.[44] The platelet count was below 150,000 in 97 per cent of the patients with APL at the time of diagnosis and below 50,000 in 78 per cent. This is a more severe thrombocytopenia at the time of diagnosis than is usually seen in acute granulocytic leukemia.[44]

Coagulation abnormalities in APL have been noted by numerous authors. Originally this coagulopathy was believed to be due to excessive fibrinolysis (reported in 5 out of 7 cases where laboratory evidence was sought), but it is now apparent that it is related to DIC. Table 2 illustrates the results of initial coagulation tests in the patients with APL reported in the literature. Although 4 patients had normal levels of fibrin degradation products (FDP) at the time of diagnosis, these become abnormal when repeated later on in the illness. Elevated FDP combined with an abnormal bleeding time, prothrombin time, thrombin time, thrombocytopenia and hypofibrinogenemia have commonly been observed. The levels of specific coagulation factors have been variable. Only factor V levels have been regularly reported and have been low in 58 per cent of patients. While DIC has been reported in other acute nonlymphoblastic leukemias, it is much less common and only rarely has clinical implications.[47,49]

APL has been reported in the blastic crisis of chronic granulocytic leukemia,[21] and in a patient with Hodgkin's disease who had been previously treated with radiation therapy.[25] One of the reported cases of APL was presumed to have been induced by thorotrast dye,[32] and APL has been reported in pregnancy[39] and in hemophilia.[36] There has been one patient with central nervous system involvement by APL, demonstrated during life.[33]

Of reported cases of APL, 79 per cent have died as a result of hemorrhage, and of these the majority have died from intracranial bleeding. Other causes of death have included infection (16%) and miscellaneous causes (e.g. cachexia, renal failure) (5%). Boggs reported hemorrhage as a cause of death in 51 per cent of patients with acute granulocytic leukemia,[44] but in recent years hemorrhage has declined as a cause of death as blood component therapy has become more widely available. At the present time most patients with acute leukemia die of infections. The predominance of hemorrhage as a cause of death in APL is one other manifestation of the serious hemorrhagic diathesis in this disease.

Until recently APL had the poorest prognosis of the acute leukemias, with most patients dying within 30 days of diagnosis, and with only an occasional patient surviving longer than 4 months regardless of therapy. In recent years this entity has responded to aggressive chemotherapy, but the major problem has been coping with the hemorrhagic diathesis during the initial stages of chemotherapeutic intervention. Daunomycin has been suggested to be particularly effective in APL.[11] Remissions have been noted with other agents (e.g. Cytosine-Arabinoside), however. The current most effective remission induction regimen includes combination chemotherapy (with particularly Daunomycin and/or Cytosine-Arabinoside), along with aggressive treatment of disseminated intravascular coagulation with heparin, and factor replacement if necessary.[42] It seems to be important to eliminate as rapidly as possible the malignant cells which are providing the source for the DIC. Using this type of regime Bernard et al reported complete remissions in approximately 50 per cent of 38 patients with APL.[41] There is some evidence that when remissions in APL do occur they last longer than in other types of acute non-lymphoblastic leukemia.[41]

APL thus is sufficiently different from other acute non-lymphoblastic leukemias in its clinical and laboratory manifestations to be recognized as a distinct subgroup of AGL (Table 3). The diagnosis of APL requires the presence of atypical promyelocytes with prominent dark staining granules, often containing Auer rods and with a peculiar structure under the electron microscope. These atypical promyelocytes should comprise the majority of the leukemic cells. The second constant feature of this disease is its accompaniment of stigmata of DIC. The devastating clinical consequences of this process constitute the most practical reason for recognizing APL. The diagnosis should be made cautiously or not at all in the absence of either of the above. It is important to recognize this disease, because although APL is at least as responsive to treatment as the other nonlymphoblastic acute leukemias, failure to quickly recognize and aggressively treat the associate coagulopathy will certainly prove rapidly fatal.

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Summary

Acute promyelocytic leukemia is a variant of acute non-lymphoblastic leukemia characterized by the presence of atypical promyelocytes in the bone marrow and peripheral blood and the syndrome of disseminated intravascular coagulation. The disease has been manifested in the past by a rapid course to death, but a review of current literature suggests there is an improved prognosis when aggressive antileukemic therapy is combined with treatment of disseminated intravascular coagulation. Other characteristics of the disease include a lack of predominance in males and older age groups, infrequent organomegaly or lymphadenopathy, prominent hemorrhagic manifestations, a tendency to leukopenia, and death usually caused by bleeding. •

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* Because of limitation of space this list of 55 references has been abbreviated by omitting those references which were entered primarily to identify reports of a case or technic of a laboratory examination. The complete reference list may be obtained from author.

The Vietnamese Orphan

A Recent Arrival

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Burris R. Duncan, MD, Peter F. Kohler, MD,
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RECENT WORLD EVENTS HAVE led many American families to adopt young Vietnamese children. Over 500 children have been screened in Denver since April, 1975, many destined for adoption throughout the United States and Europe. A large number of these children will be living in the mountain states area and their health care will become the responsibility of practitioners in this region. To permit a more complete evaluation of these youngsters, information is presented concerning their initial medical evaluations.

Laboratory data from initial evaluations in receiving homes was collated on 144 children. Information was incomplete on many of these because of difficulties in specimen collection and data retrieval and the rapidity with which some children were placed for adoption. In addition, hospital charts on thirty-six of thirty-seven children hospitalized in three major pediatric in-patient units in Denver were reviewed. This group included four children in the larger group of 144, while the remainder of the hospitalized children had no initial screening data available.

Initial Screening

Although no age or sex breakdown was available, the majority of the children were under one year of age with approximately equal numbers of males and females. Children in general were found to be in good health, suffering primarily from mild malnutrition, diarrhea, otitis media, scabies, impetigo, and thrush. A few of the children had injuries stemming from the infamous plane crash in Saigon during the evacuation.

Laboratory data was available on 144 of the children evaluated in receiving homes. Over 50 per cent of the children were found to have mean corpuscular volumes (MCV) below American standards. Eosinophilia was noted in 14.5 per cent of the children, although only 1 of 13 stools examined for ova and parasites was positive, that specimen revealing *giardia lamblia.* Hepatitis B surface antigen (HB_SAg) was demonstrated in 9.0 per cent of the children, while slightly less had specific antibody to HB_SAg (anti-HB). Liver enzymes as measured by SGOT were elevated in 6.5 per cent, only 2 of the 8 abnormal values being in children with HB_SAg. Three children had reactive VDRL's, only one of these having a positive FTA-ABS. Of 16 chest x-rays, none were suggestive of tuber-

TABLE 1
Laboratory Data at Initial Evaluation at Receiving Homes

Test	No.	No. Abnormal	Percent
Mean Corpuscular Volume ($<82\ u^3$)	89	52	58.4%
Stool Cultures	66	12*	18.2%
Eosinophilia ($>700/mm^3$)	62	9	14.5%
HB_SAg	144	13	9.0%
anti-HB_S	85	7	8.2%
Ova and Parasites	13	1	7.7%
SGOT	124	8	6.5%
VDRL	64	3	4.7%
Malaria smear	109	0	.0%

* Salmonella-9; Shigella-3

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TABLE 2
Reason for Hospital Admission

INFECTION		34
Temperature Instability	6	
+ Diarrhea ± Dehydration	19	
+ Respiratory Distress	5	
+ Measles	1	
Diarrhea	2	
Abscess	1	
HERNIA	1	1
ANXIETY REACTION	1	1
TOTAL		36

culosis. Stool cultures were positive in 18.2 per cent of the 66 cultures performed as a screening measure. Nine of these were salmonella, the majority being Salmonella *senftenberg*(E_4) sensitive only to gentamicin and trimethoprim-sulfamethoxazole. Smears for malaria were done on 109 children with none being positive (Table 1).

Hospitalized Children

Thirty-six children or 6 per cent of the total population screened in Denver required subsequent hospitalization in Denver. Some of the children had been hospitalized prior to arrival in Denver suggesting that a larger per cent were ill enough to require treatment in a hospital at some stage of the evacuation process. An additional number will need hospitalization early in their adoption. The average age of the thirty-six patients for whom information is available was 12 months while the median age was 3 months. Ninety-four per cent of the admissions were for infections (Table 2).

Laboratory data obtained on the hospitalized patients was roughly comparable to that discussed earlier. As with the total population, anemia was present in over 50 per cent of the hospitalized group and scabies was diagnosed in nearly 60 per cent. Over two-thirds suffered from diarrhea and nearly that many had clinical evidence of some malnutrition. One-third of the children had stool cultures positive for salmonella and/or shigella. Only one in thirty children whose stools were examined for ova and parasites was positive, that specimen having *Entamoeba histolytica.* One of 13 VDRL's done during the hospitalization was associated with a positive FTA-ABS. Twelve of 22 chest x-rays were suggestive of a viral pneumonitis; none were compatible with tuberculosis (Table 3).

One death occurred, that being secondary to complications of *pneumocystis carinii* pneumonia.

Discussion

Although it is apparent that these Vietnamese orphans have a myriad of health problems, none pose an unusually significant health risk in the United States. It is however imperative that health professionals be aware of the incidence of diarrheal diseases, tuberculosis, and carriage hepatitis B surface antigen (HB_SAg) in this population. Limited data is available concerning disease incidence in Vietnam, but some surveys have documented that salmonella and/or shigella are present in about 20 per cent of specimens from symptomatic children under 5 years of age.[1] The incidence of tuberculosis is unknown in the Saigon area, although 11.3 per cent of the children less than 15 years of age screened in the refugee programs currently underway had positive PPD skin tests.

TABLE 3
Medical Problems of Hospitalized Children (N=36)

GENERAL		
Malnutrition		24
Hepatosplenomegally		13
INFECTIONS		
Scabies ± Pyoderma		21
Diarrhea ± Dehydration		26
Non-specific	14	
Salmonella E	8	
G	1	
Shigella D	1	
Salmonella B + Shigella B	1	
Salmonella E + Shigella B + Entamoeba histolytica	1	
Otitis Media		14
Thrush		12
Upper Respiratory Infections		12
Pneumonia		13
Pneumocystis carinii	1	
Empyema (E. coli)	1	
Conjunctivitis		5
Group A Strep		4
Varicella		2
Measles		2
Reactive VDRL's (one false positive)		2
Shoulder Abscess		2
Positive HB_SAg		1
Presumptive tuberculosis		1
HEMATOLOGIC		
Anemia		19
Neutropenia		1
Thrombocytopenia		1
MISCELLANEOUS		
Heart Murmur		6
Cleft Lip and Palate		1
Hernia		1
Anxiety Reaction		1

Only twelve of 12,841 had suspicious chest x-rays and none had a positive sputum for mycobacteria. BCG vaccination is frequently given in Vietnam and the positive skin test thereby produced may partially account for this incidence.[2,3] Within the orphan population screened in Denver, only one case of presumptive tuberculosis was diagnosed.

Parasitic infections are thought to be prevalent in Vietnam, but examinations in Denver showed few pathogens.[4] Cases of both *vivax* and *falciparum* malaria have been reported in refugees, but all smears have been negative in the orphan population. Similarly, cases of measles, chicken pox, diphtheria, pertussis, typhoid, hepatitis, and dengue have been documented in the refugee population.[3]

Within the orphan population screened in Denver, there were multiple cases of measles, chicken pox, salmonella, shigella, and positive cultures for Group A streptococcus. Only 9.0 per cent of the screened population had hepatitis B surface antigen (HB_SAg) in contrast with 27 per cent noted among older Vietnamese children adopted between 1967 and 1972. This lower per cent may reflect the young age of the orphan group, Stevens et al recently reporting vertical transmission up to 6 months of age.[5] The one death in our group was secondary to complications of *pneumocystis carinii* pneumonia, and informal reports suggest that this is a significant problem in this group.[6]

In view of our initial experience, it is recommended that routine well-child care be supplemented by a battery of screening tests to define the presence or absence of ongoing illnesses. These should include complete blood count, VDRL (and FTA-ABS if positive), and hepatitis B surface antigen (HB_SAg) initially, and at 6 months of age, SGOT, tuberculin skin test, and stool specimens for culture and ova and parasite examinations. Malaria smears need only be considered in the presence of compatible illnesses, and chest x-rays indicated only with respiratory symptomatology or positive skin tests. Immunization status should be reviewed and updated.

It is evident that the medical problems encountered in caring for Vietnamese orphans are not unique to that population. However, these children require careful screening and prompt attention to their nutritional and health status to facilitate rapid acculturation into their adopting families. •

ACKNOWLEDGMENT

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Mumps Meningoencephalitis*

A Possible Clue to Early Diagnosis

**Frederic W. Bruhn, MD, Paul M. Mendelman, MD, and
Jules Amer, MD, Denver**

PRONOUNCED PLEOCYTOSIS WITH A HIGH per cent of lymphocytes characterizes the cerebrospinal fluid (CSF) of patients with mumps meningoencephalitis. In certain patients, however, with well documented mumps meningoencephalitis, the CSF profile may reveal a predominance of polymorphonuclear cells, a low sugar or a moderately elevated protein.[1,2] In patients without parotitis who have received antibiotics prior to lumbar puncture, the CSF profile may, on occasion, be confused with that of patients with partially treated bacterial meningitis.[3]

We recently cared for a patient who demonstrated the possible value of the combination use of the soluble (S) and viral (V) complement fixing antibody determinations in the differential diagnosis on a single acute serum specimen.

CASE REPORT

A 6-year-old Spanish American boy was admitted to Denver Children's Hospital with meningitis of unknown etiology. He had enjoyed excellent health until 10 days prior to admission when he experienced fever of 104°, anorexia, vomiting, and a right frontal headache. His physician treated him with CR Bicillin 600,000 units I.M. followed by Penicillin G 125 mg P.O. t.i.d continuously until 2 days prior to admission. High fever persisted intermittently for 6 days followed by a low grade temperature. Intermittent delirium was reported. The patient was brought to the Emergency Room on the day of admission because of persistent malaise.

Past history disclosed no prior serious illness. Several classmates had had mumps 1 to 2 weeks before the patient became ill. The patient had no past history of mumps and had not received the mumps vaccine.

Examination on admission showed a lethargic weak 6-year-old male with temperature of 99.6° F, pulse of 108/minute and respiratory rate of 20/minute. Definite signs of meningeal irritation were present without evidence of focal infection elsewhere. Questionable hyperemia of Stenson's duct was present without definite parotid swelling.

Laboratory data on admission included a white blood count of 4800/mm^3 with 40% PMN's, 59% lymphs and 2% mononuclears. Sedimentation rate was 31 mm/hr. Initial CSF showed a WBC count of 467/mm^3 with 8% PMN's; CSF glucose was 30 mg% with a concomitant blood sugar of 86 mg%; CSF protein was 740 mg%. Subsequent CSF values as well as serial mumps serology, are shown in Table 1. Serum electrolytes were within normal limits and a Mono spot test was negative. The serum amylase on two separate occasions were 55 and 47 Close Street units (normal: 6-33). The chest x-ray was within normal limits. Intermediate PPD skin test was negative. Nasopharyngeal culture yielded a non-typable *Hemophilus influenzae*, but blood and CSF cultures remained negative. Cultures taken on the third hospital day (13th day of illness) of nasopharynx, throat, rectum, urine and spinal fluid were inoculated into Rhesus monkey kidney, HEp-2 and fetal lung for viral isolation. No virus was isolated. Mumps viral (V) antigen for the CF test was obtained from Flow Laboratories and Mumps Soluble (S) antigen was produced by Lederle Labs. Paired sera showed no rise in antibody titer to WEE, St. Louis Encephalitis, California Encephalitis and Influenza A and B. Brain scan and EEG performed early in the hospital course were within normal limits.

Because of the initial confusing clinical picture, the history of prior penicillin therapy, and the initial low spinal fluid glucose and very high protein, a diagnosis of partially treated bacterial meningitis was made, and the child was placed on intravenous Ampicillin 300 mg/kg/day divided q 4 hours. Over the next several days gradual improvement occurred and the patient was discharged after completing a 10 day course of Ampicillin. Subsequent visits to the outpatient department continue to show a healthy boy with no obvious sequelae.

TABLE 1

Day after onset of illness	Cerebrospinal Fluid					Reciprocal of Mumps CF antibody	
	WBC /mm^3	PMN's %	RBC /mm^3	glucose/ bl. gl. (mg %)	protein (mg %)	S	V
10	467	8%	88	30/86	740	64	8
12	582	5%	37	30/88	610	128	8
20	96	4%	9	28/80	130	128	64
33	100	0%	1	41/73	84	128	64

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* From the Department of Pediatrics, University of Colorado Medical Center and the Children's Hospital, Denver, Colorado. This study supported in part by PHS Training Grant HD-65. Reprint Address: Frederic W. Bruhn, MD, Department of Pediatrics, Denver General Hospital, Denver, Colorado 80204.

Discussion

When meningoencephalitis occurs in association with parotitis, the diagnosis of mumps is readily suggested. However, when parotitis is not obvious, as occurs in as many as 50 per cent of reported cases, the differential diagnosis is more difficult,[4,5] and is usually made by the isolation of mumps virus or by the demonstration of significant rises in antibody as measured by a complement fixation or hemagglutination inhibition test.

Isolation of mumps virus requires a diagnostic virology laboratory and is often difficult by the time the patient presents with meningoencephalitis, as in our case.[6] Serologic diagnosis utilizing paired sera requires several weeks and is thus not helpful in making clinical decisions regarding the initial management of the patient. Similarly, measurement of the serum amylase to determine whether this test would identify patients with mumps meningoencephalitis without parotitis usually has been unrewarding.

In 1947, Henle et al reported the finding of two serologically distinct antigens derived from chicken embryos infected with mumps virus which fixed complement.[7] These were termed V (viral) antigen and S (soluble) antigen. Subsequent reports demonstrated the usefulness of using both antigens in making a presumptive serologic diagnosis of a recently acquired mumps on a single specimen of serum.[8,9] Frequently, serum obtained near the onset of illness contains antibody to S antigen and contains little antibody to V antigen. During convalescence, antibody to both antigens attains a high titer. Our patient demonstrated the pattern of high S (1:64) and low V (1:8) on his initial serum. His diagnosis was subsequently confirmed by a significant complement fixation titer rise against the more widely used viral (V) antigen. If the S and V antibody pattern had been measured at the onset of illness, the diagnosis of mumps meningoencephalitis might have been made and administration of intravenous antibiotics and a prolonged hospitalization might have been avoided. Cross reactions with paramyxoviruses may occur and elevation of titer to the S antigen may be due to recent infection with another paramyxovirus. However, in the clinical setting with meningoencephalitis, these other viruses would be uncommon etiologic agents.

The S and V antigens are commercially available. The test can be done in 24 hours by any laboratory equipped with materials for performing a standard complement fixation test.

Summary

A case of mumps meningoencephalitis with a low CSF glucose and an extraordinarily high CSF protein, without parotitis, and simulating partially treated bacterial meningitis is presented. Increased use of the soluble (S) antigen complement fixation antibody test in combination with the standard viral (V) antigen on a single acute sera would facilitate an early diagnosis in certain individuals. •

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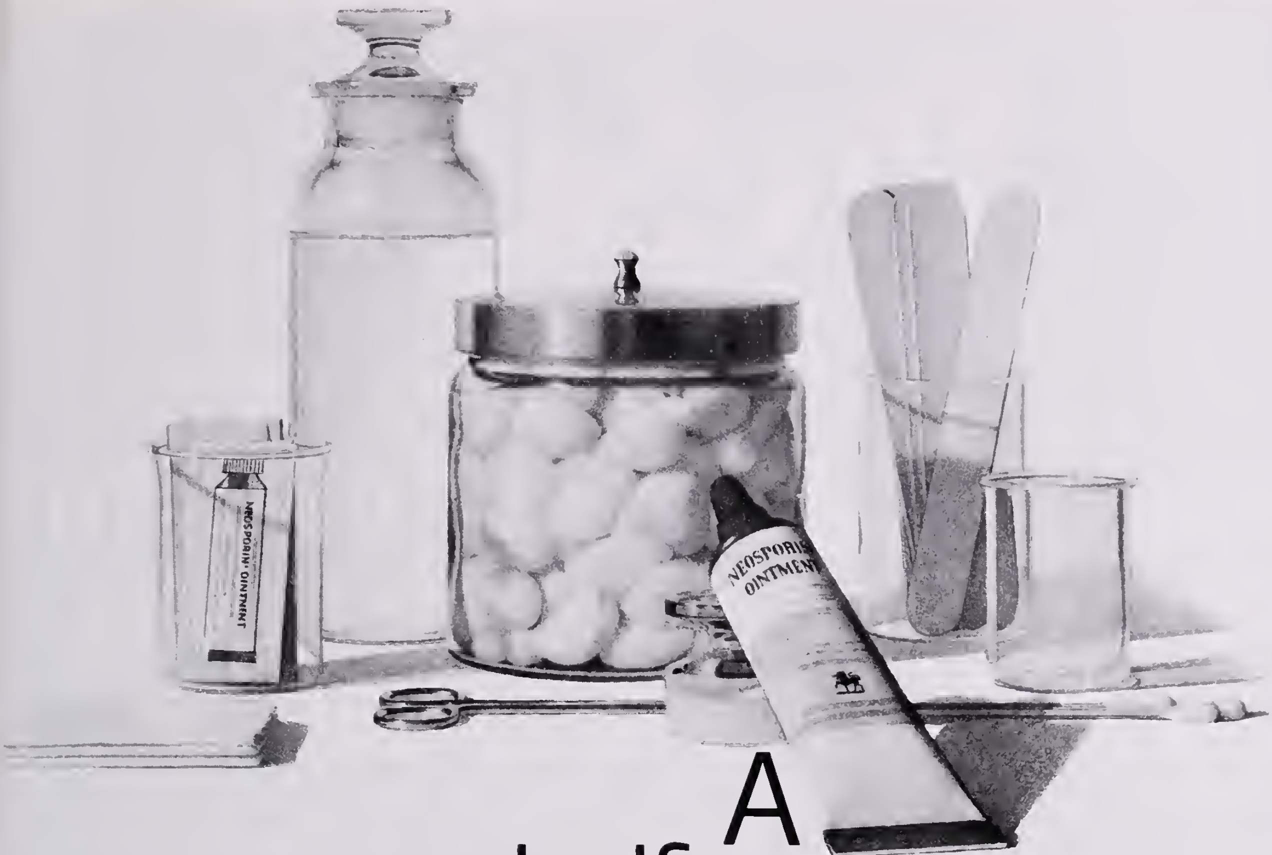

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WARNING: Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

PRECAUTIONS: As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

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Complete literature available on request from Professional Services Dept. PML.

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COLORADO

Leukemia Grant to Denverite

Clark Anderson, MD, of the National Jewish Hospital and Research Center has been named a Special Fellow by the Leukemia Society of America, Inc., and will receive $31,000 over a two-year period to support searches for cures for leukemia and allied diseases of the blood-forming organs.

Barnes Scholarships Memorial

Scholarships of $1,000 each have been established at the University of Denver by Broda Barnes, MD, of Fort Collins in the memory of William McConnell, MD, and Reuben Gustavson, PhD, both DU graduates. McConnell practiced in Monument, and Gustavson was chairman of the DU chemistry department, president of the University of Colorado, and chancellor of the University of Nebraska. Dr. Barnes is a 1928 graduate of the University of Denver.

Cancer Center Funding Arrives

Colorado Regional Cancer Center, Inc. (CRCC) has received official notification of the National Cancer Institute's funding, according to Charlene P. Holton, acting executive director of CRCC and director of pediatric oncology at Denver Children's Hospital.

The Colorado Regional Cancer Center (CRCC) was incorporated as a private, non-profit corporation in April, 1974, and in June of that year was designated by the National Cancer Institute as one of the nation's 17 comprehensive cancer centers. The Cancer Center plans to work with hospitals, doctors and researchers throughout the region in the effort to fight cancer.

One of CRCC's purposes is to make available to the citizens of the Rocky Mountain area the most up-to-date diagnostic and therapeutic anti-cancer methods and initiate educational and demonstration programs through the various cooperating centers in the region.

CRCC's president is George M. Hopfenbeck, Jr., a local attorney. Vice Presidents are Samuel Butler, Jr., President of Sharples Oil Company and Harry P. Ward, MD, Dean of the University of Colorado Medical School. Members of the Executive Committee include Don Friedman, Alexis E. Lubchenco, MD, Bishop George R. Evans, Rabbi Manuel Laderman, Mrs. Carol P. Tempest and F. Clifton Schmidt, and the board's 23 members include prominent business people from the area as well as physicians and scientists.

Farr Honored by Chicago

Richard S. Farr, MD, chairman of the Department of Medicine at the National Jewish Hospital and Research Center and professor of medicine at the University of Colorado Medical Center, has received a Distinguished Service Award from the University of Chicago Medical Alumni Association. Dr. Farr received his MD from the University of Chicago in 1946.

Duncan to HOPE

Burris Duncan, MD, pediatrician at the University of Colorado Medical Center goes to Natal, Brazil in August to join the staff of Project HOPE. Duncan served with Project HOPE in Maceio, Brazil in 1973; he will remain until February 1977.

MONTANA

Tkach Library Moves

The Trustees of the John R. Tkach, MD Educational Trust announce that the Helen G. Tkach Memorial Dermatology Tape library will be moved on July 1 to Bozeman, Montana. The library now consists of over 300 tapes of lectures and seminars in Dermatologic basic and clinical sciences. The new location of the library will be The John R. Tkach, MD Educational Trust, Route 4, Box 60, Middle Creek Road, Bozeman, Montana 59715. Tapes are available on free loan; Montana Dermatologists may contact Dr. Tkach. Colorado doctors still using tapes are asked to return them by mail to the Montana address.

NEVADA

Nevada

Ernest W. Mack, MD, former chairman of the Washoe Medical Center board of trustees, Reno, and a member of that board for 26 years, was recently elected vice president of the American Association of Neurologic Surgeons. Dr. Mack was named in November to be vice president of the American Academy of Neurologic Surgeons, and serves as secretary of the American Medical Association neurosurgical section.

MEDICAL SCHOOL NOTES

University of Colorado Medical Center

New Post for Marine

William M. Marine, MD, currently chairperson of an Interdisciplinary Group in Community Health and Health Care Delivery at Emory University School of Medicine, Atlanta, Georgia, has been named chairman and professor of the Department of Preventive Medicine and Comprehensive Health Care at the University of Colorado Medical School. A recipient of an MD degree from Emory University, he has a master's in public health from the University of Michigan. He will assume his new position September 1, 1975.

University of New Mexico Medical Center

Greenberg to Chair Pediatrics

Robert Greenberg, MD, presently chairman of the pediatric department at the Charles R. Drew Postgraduate Medical School, professor of pediatrics at the University of California, Los Angeles, and pediatrician-in-chief at the Martin Luther King, Jr. Hospital in Watts, has been named chairman of the department of pediatrics at the University of New Mexico School of Medicine.

Wiese Heads Department

William H. Wiese, MD, acting chairman of the department of family and community medicine at the University of New Mexico School of Medicine for the past two years, has been named chairman of the department. Dr. Wiese serves in many capacities including director of Project Porvenir, director of the preceptorship program in primary care, director of the Navajo Area Health Education Center, and director of a project to develop a Rural Health Resources Center. He chairs both the public health committee of the Albuquerque and Bernalillo County Medical Association and the New Mexico Medical Society Rural Health Committee.

Moseley Receives British Honor

Robert D. Moseley, Jr., MD, assistant chairman of the UNM medical school's radiology department, was named the first honorary fellow of the English Royal College of Radiologists following his address that inaugurated the Royal College of Radiologists. Queen Elizabeth II recently chartered the former Faculty of Radiologists as the Royal College of Radiologists, and Dr. Moseley was given a unanimous invitation by the British members to deliver the inaugural address.

FAMILY PRACTICE

Suburban Denver has excellent private practice opportunities for family physicians.

All family physicians, including those from within the Metropolitan Denver area, are invited to explore the potential for development of additional quality health care in expanding suburban Aurora.

HUMANA, the national hospital company, has recently opened a 200-bed full service hospital in southeast Denver. **AURORA COMMUNITY HOSPITAL,** whose service area includes Arapahoe and Adams Counties, is playing a vital role in meeting the growing health care needs of the people in this area.

An adjacent 30-suite Professional Building is soon to be completed. Come explore the potential for developing your practice. For specific information on the available opportunities, call collect, Administrator, **AURORA COMMUNITY HOSPITAL,** 303/751-5353.

105th Annual Session

COLORADO MEDICAL SOCIETY

The Broadmoor, Colorado Springs, Colorado

September 17-20, 1975

WEDNESDAY, September 17

8:00 a.m.—ORIENTATION COURSE

9:30 a.m.—HOUSE OF DELEGATES, FIRST MEETING

2:00 p.m.—REFERENCE COMMITTEE MEETINGS

THURSDAY, September 18

9:00 a.m.—NATIONAL HEALTH LEGISLATION

10:15 a.m.—PANEL DISCUSSION
Kenneth A. Platt, MD, Moderator

6:30 p.m.—RECEPTION
Hosted by Dr. and Mrs. Howard T. Robertson

FRIDAY, September 19

PROFESSIONAL LIABILITY

9:00 a.m.—James M. Vaccarino, LLB
Director of Legal Affairs
Massachusetts General Hospital

Subject: Nature of medical malpractice litigation, current trends of insurance dilemma.

9:30 a.m.—Daniel S. Hoffman, LLB

10:30 a.m.—PANEL DISCUSSION
Howard T. Robertson, MD, Moderator
Participants: James M. Vaccarino, LLB
Daniel S. Hoffman, LLB
Alden V. Hill
Chairman, Colorado Bar Association Interprofessional Committee
Robert S. Brittain, MD, Chairman, Colorado Medical Society Committee on Professional Liability

7:30 p.m.—ROARING TWENTIES PARTY, INTERNATIONAL CENTER

$15 per person, Buffet and Dancing

SATURDAY, September 20

8:30 a.m.—HOUSE OF DELEGATES, SECOND MEETING

Physicians outside Colorado are invited to attend. Make accommodation arrangements directly with The Broadmoor, Colorado Springs, 80901. For registration and other information contact: Convention Department, Colorado Medical Society, 1601 East 19th Avenue, Denver, Colorado 80218

72nd Annual Meeting
WYOMING STATE MEDICAL SOCIETY

Jackson Lake Lodge, Moran, Wyoming

Tuesday, August 26 to Friday, August 29, 1975

TUESDAY, August 26

Specialty meetings

WSMS Golf Tournament

1st Annual Wyoming AAFP Dinner

WEDNESDAY, August 27

Remarks by Wyoming Congressional Delegation

Remarks by Max Parrott, MD, AMA President

House of Delegates

Reference Committee Meetings

THURSDAY, August 28

Scientific Session:

Introductory overview of immunoglobulins, T and B lymphocytes, humoral vs. cellular immune and responses and complement.

John Leddy, MD
Division of Immunology
University of Rochester School of Medicine and Dentistry
Rochester, New York

Allergy, including IgE-mediated reactions, newer concepts of asthma and its treatment, drug reactions (especially penicillin) and probably hypersensitivity pneumonitis

John Condemi, MD
Division of Immunology
University of Rochester School of Medicine and Dentistry
Rochester, New York

Immunologic concepts in cancer and cancer therapy

Richard Reed, MD
Division of Experimental Therapeutics
M.D. Anderson Hospital,
Houston, Texas

Concepts of immune complex disease including glomerulonephritis and various types of visculitis

Edmund Lewis, MD
Department of Medicine, Renal Unit
Presbyterian-St. Luke's Hospital
Chicago, Illinois

Selected auto-immune hematologic disorders. Auto-immune hemolytic anemia, ITP drug induced hemolytic anemia, and thrombo cytogenia.

Dr. Leddy

Immunodeficiency diseases in children and adults: defects in humoral and/or cell-mediated immunity, leukocyte functiona defects, etc.

Dr. Condemi

Panel: Immunosuppressive and anti-inflammatory drugs: Mechanisms of action and complications.

All speakers

President's Annual Banquet
Speaker: The Honorable Edward Herschler, *Governor of Wyoming*

Physician of the Year Award

FRIDAY, August 29

House of Delegates: Action on malpractice insurance
Presentation of new Wyoming Blue Cross Fee Schedule

Election of WSMS Officers, Nomination of Blue Cross and Blue Shield Trustees

NATIONAL AFFAIRS

Summary of Actions of The House of Delegates American Medical Association 124th Annual Convention Atlantic City, New Jersey June 14-19, 1975

In the most momentous session to be held in decades, delegates at the 124th Annual Convention in Atlantic City urged vigorous AMA action in a number of medical problem areas—including malpractice and federal intervention—and then approved a substantial dues increase to assure the necessary financial support.

Meeting for 22 hours and 37 minutes, the longest Convention in recent memory, the House acted on 73 reports and 168 resolutions for a total of 241 items of business.

Repeatedly emphasizing stronger AMA involvement in confronting problems facing local physicians, an overwhelming majority of the House voted to raise annual dues of regular members to $250, intern-resident dues to $35, and to maintain student dues at $15.

(For more information on dues increase and related matters such as changes in AMA organizational structure, malpractice proposals and actions to forestall unreasonable government intervention in medicine see "Association and Internal Matters of the House", "Physicians and Government", and "Physicians and the Public".

Elections

Delegates selected Richard E. Palmer, of Alexandria, Va., as president-elect. Others elected or re-elected to positions in the Association were:

Vice-President: George W. Slagle, Michigan

Speaker of the House: Tom E. Nesbitt, Tennessee (re-elected)

Vice-Speaker of the House: William Y. Rial, Pennsylvania (re-elected)

Trustees, for 3-year terms: Joe T. Nelson, Texas (re-elected); Robert Hunter, Washington (re-elected); Jere W. Annis, Florida (re-elected); Joseph M. Boyle, California. For the unexpired two-year term of Richard E. Palmer, named President-Elect, Lowell H. Steen, Indiana.

Special Citation—Leo E. Brown, formerly Special Assistant to the Executive Vice-President, was presented with a special citation for 25 years of service to the AMA.

Summary of Actions of the House of Delegates

Because of the varied nature of the actions taken by the House, and for the sake of clarity, this summary will be divided into five subject areas with appropriate sub-headings as follows:

—Association and Internal Matters of the House
—Physicians and the Government
—Physicians and the Public
—Physicians and Hospitals and Medical Schools
—Miscellaneous

Association and Internal Matters of the House

Dues Increase and Related Priorities—In increasing annual dues of regular members from $110 to $250, delegates also served clear notice of a new and aggressive stance by the AMA in dealing with the many problems facing the nation's physicians.

In just one of the problem areas discussed—malpractice—the House called for the AMA to take immediate actions to help ease the crisis, including the formation of an AMA-sponsored professional liability reinsurance company.

The company will provide backup or second-level coverage for those state medical societies that have sponsored their own medical liability insurance programs.

(For more details on this and other actions urged by the House to combat the malpractice crisis see "Physicians and the Public".)

Meanwhile, delegates unanimously endorsed a substitute resolution applauding the recent suit filed by the AMA against HEW regulations which mandate post-admission certification of hospital patients, and left no doubt that a primary reason for approving the dues increase was to provide fiscal support not only for the present suit, but for similar actions as well. Thus the second resolve of the resolution reads:

"That the Board be encouraged to continue to take such action in the future on further legislation or government regulations that threaten the ability of physicians to provide quality medical care to patients".

The House was appraised of the fact that Trustees have instructed the AMA Office of General Counsel to lay the legal groundwork for possible suits against the new federal health planning program, HEW regulations for the proposed "Maximum Allowable Cost" purchase of drugs, and for objectionable features of proposed health manpower legislation should those features be enacted.

In other priorities related to the dues increase, the House called for continuing efforts to re-build the AMA on a sound financial basis, and strongly supported a reshaping of the AMA publishing program as well as a restructuring of the organization itself.

By adopting the $250 dues level recommended by the Board, the House was assured that depleted financial reserves would be restored, that present programs would be continued, and that additional programs—such as those for malpractice and to combat growing government presence—would be mounted. In related actions, the House called for:

—Balanced budgets in both accounting and program formats.

—Intensified membership recruitment and retention efforts.

—Continued administrative support of AMPAC.

—Annual reports on the status of AMA fixed assets and investments.

Advertising-Publications—Acting on further information provided by the Special Committee of the House appointed at Portland last December, delegates endorsed "a policy of aggressive advertising promotion" in AMA publications and asked the Board to implement this policy at the earliest possible time.

In other actions, the House urged that the 10 specialty journals be placed on a self-sustaining subscription basis, or that appropriate arrangements be reached with the specialty societies involved.

Upon questioning by trustees, however, the House made it evident that it will be left to the Board to determine the eventual fate of *Prism*, so long as the disposition is to the financial advantage of the AMA.

This interpretation emerged as the result of a special consultants' report to the House on Sunday, June 15, when it was pointed out that AMA publications are valuable properties which should be handled like other Association assets.

In short, *Prism* could be sold, or it could be continued if it could be put on a paying basis.

The House also authorized the Board to set subscription rates for all publications—including *Today's Health*, excepting only *JAMA* and *American Medical News*.

Organizational Structure—The House endorsed the concept of restructuring the AMA, including Councils and Committees, and directed its Council on Long Range Planning and Development to submit a definitive report at this fall's Clinical Meeting in Honolulu.

Key elements in the report are expected to be the 1975 AMA Plan, and its clustering of AMA priorities into five major areas: organizational structure; resolving the malpractice crisis; fighting increased government intervention; maintaining AMA's leadership role in medical education; and strengthening AMA resources.

The Special Committee of the House also has recommended a more compact council-committee structure aimed at medical education, medical practice, scientific activity, internal activity, and external activity.

In other actions on Association and Internal Matters, the House

—Adopted a resolution to permit newly-elected delegates to begin their terms on January 1 or on July 1 at the discretion of state societies.

—Amended the delinquency provisions of the Constitution and Bylaws to include future assessments, as well as dues.

—Urged constituent societies to provide full membership privileges for medical students at nominal dues.

—Approved a set of model membership bylaws for distribution to constituent societies.

—Asked the Board to consider the establishment of a Section on Nuclear Medicine through appropriate mechanisms.

—Endorsed the re-establishment of AMA-AMPAC workshops on a self-sustaining fiscal basis.

—Commended the Board of Trustees, officers and staff for displaying fiscal responsibility in meeting the financial crisis of the last 18 months.

Physicians and the Government

Reimbursement Under Government Health Programs—The House strongly reaffirmed the AMA's long-standing position that physicians participating in government health insurance programs should be reimbursed on the basis of usual, customary and reasonable charges.

In a further step, Delegates requested the Council on Medical Service to examine the Medicaid and Medicare programs to see if reimbursement did meet AMA policy, and to report back at the Honolulu Clinical Meeting.

The House also adopted report JJ of the Board, which updates Board actions in objecting to the proposed payment of usual, customary and reasonable Medicare fees based on a national economic index as recently promulgated in regulations published in the Federal Register.

The Board report emphasizes continued and vigorous opposition to the proposal, including legal action should it become necessary.

Federal Health Planning Program—The House unanimously supported the Board in its recent actions to oppose implementation of the National Health Planning and Resource Development Act enacted by the last Congress.

The delegates pledged support for "any action, including a legal action" that the Board deems appropriate and effective in preventing implementation of the new planning law.

PSRO Policy Reaffirmed—Delegates reaffirmed present AMA policy on PSRO's, and defeated a call for repeal of the PSRO law. After discussion in reference committee and on the floor of the House, delegates reaffirmed PSRO policy adopted at the 1974 Annual Convention.

The policy basically calls for AMA action to seek constructive amendments to the law and appropriate regulations and directives, and to support continued monitoring of the program. The policy also holds that should the PSRO program become too restrictive, however, the Board can seek repeal. And here again, the House cited the possibility of legal opposition if it becomes appropriate.

In a related development, the House requested the Board to prepare a detailed breakdown of expenditures for the federally-funded program under which the AMA is developing PSRO practice criteria, and make them available to members of the House on request.

In other actions related to peer review, Delegates urged physicians to "continue to perform peer review directed at increasing the quality of patient care and reducing its cost," and also urged physicians not to seek compensation for non-government peer review participation as established in hospitals. The Board endorsed compensation for government-connected peer review programs, however.

Other House recommendations related to Physicians and the Government included:

—That the AMA seek repeal of an amendment to federal law which equates psychologists and optometrists with physicians in the provision of medical care to government employees under health insurance programs.

—That the AMA seek appropriate changes in federal health insurance programs to make the basis for physician visits to nursing homes real medical need rather than regulatory requirements.

—That the AMA continue its efforts for adoption of the AMA's Current Procedural Terminology in government health programs.

—That the Board speed up efforts to rectify abuses in the promulgation of regulations in the Federal Register.

Physicians and the Public

Professional Liability Proposals—In endorsing a series of proposals aimed at mitigating malpractice problems, the House stressed that the continued ability of physicians to provide care to patients was a prime motivating factor.

While adopting a substitute resolution supporting the use of "all available legal means" by local physicians in seeking reforms in professional liability insurance, for example, it was emphasized that work slowdowns were basically a commitment to continued patient care rather than personal financial gain in the traditional sense of a strike.

The final version of the resolution reads: "The AMA recognizes that physicians are entitled to use all available legal means, without jeopardizing the medical care of their patients, to protest when intolerable and unwarranted burdens are placed upon their patients, the Association, or its members".

The resolution also recognizes that "the primary commitment of the AMA and its physician members is to the essential medical needs of the people of this nation".

In other actions aimed at easing the malpractice crisis, the House urged early establishment of an AMA-sponsored professional liability reinsurance program so as to provide a second level of protection for state society-sponsored primary insurance plans.

As a condition of participation, states with captive carriers would have to effect changes in the state tort system to insure long-range improvements in the underwriting climate.

In other malpractice actions, the House urged renewed AMA assistance to state societies in seeking legislative enactment, and public endorsement of, mechanisms such as voluntary arbitration plans, and changes in tort law to relieve statutory elements which contribute to malpractice problems.

The House also reaffirmed its stand against claims-made types of insurance coverage, and voted to encourage the federal government to provide coverage for physicians employed by government.

National Health Insurance—Delegates supported the national health insurance bill of the AMA which has been introduced in Congress. The bill would provide both basic and comprehensive benefits for all Americans, but would minimize federal administration and financing.

During a health insurance debate in the House, considerable sentiment was expressed for a national catastrophic insurance coverage program, but the subject was referred to the Board for further study.

In other actions related to Physicians and the Public, the House:

—Urged measures to assure physicians and patients of high-quality drug therapy by seeking possible modifications in FDA regulations to facilitate improvements in the development and distribution of drugs.

—Called for expanded use of flame-resistant fabrics in clothing, bedding, draperies and decorative materials to reduce burn hazards.

—Reaffirmed existing policy in lieu of a resolution that would have defined death as "irreversible cessation of total brain function", which present policy defines as one acceptable criteria.

—Endorsed legislation to permit Social Security recipients to earn unlimited income without a reduction in retirement benefits.

Physicians and Hospitals and Medical Schools

Medical Staff Prerogatives in Patient Care—Several actions aimed at preserving hospital medical staff prerogatives in patient care were endorsed by the House.

A joint report of the Councils on Medical Education and Medical Service provided a detailed study of possible medical staff problems posed by the increasing appointment of salaried chiefs of staff and department heads by hospital governing bodies.

The report pointed out that medical staff rights and prerogatives could be thus shifted to governing boards, and made several recommendations for local medical staffs and medical societies to counter the trend. Delegates adopted the report.

The House also endorsed a Board report urging AMA members on the Joint Commission on Accreditation of Hospitals to seek to amend JCAH standards to provide due process for physicians employed in medico-administrative positions.

In related actions, Delegates supported measures to prevent local or regional duplication of JCAH functions, and urged that JCAH be requested "to limit requirements for medical audit or other quality assurance activities by medical staffs" to those whose necessity can be "documented" by the AMA Board of Trustees.

Foreign Medical Graduates—The House endorsed a continuation of the fifth pathway concept of the AMA for determining the qualifications of FMG's, rejecting a proposal to eliminate the program.

Medical Schools—The House voted to continue opposition to medical manpower legislation now before Congress which would require medical students to repay capitation grants to their schools or else provide "in-kind" service in areas stipulated by government, and which would provide federal control of the number and distribution of residencies.

Inaugural Address, Max H. Parrott, President of AMA

In his inaugural address on Wednesday, June 18, Dr. Max H. Parrott, the new AMA president, said that "the great national debate on health and medical issues is a clash between (government) utilitarianism and (medical) humanism".

In viewing medical care as a commodity rather than a service, Dr. Parrott said, "the health care planners and regulators see medical care as little more than a numbers game . . . If only the commodities of health care can be more efficiently organized, assembly-line style, if only the providers of care can be better coordinated as a work force, then the consuming public will be eternally blessed".

And efficiency in providing such a "commodity", Dr. Parrott emphasized, is the intent of such government programs as PSRO's and HMO's.

"But", he warned, "medically speaking, efficiency . . . optimum production at the least cost in time and money . . . means something far different from quality".

Such efficiency could in truth subvert quality of medical care, which he defined as "giving the best appropriate service . . . regardless of the time required . . . and regardless of cost".

The AMA, Dr. Parrott stressed, "has much to say about the plain truth that medical action depends on the freedom to act, rather than on regulation.

"We have so much to say about the clear prospect that in any squeeze play between federal regulators of medicine and the regulated, the patient, too, will be crushed.

"We have so much to do and say in Washington and across the land. And so little time. We want an AMA spirited enough to save the individual spirit of medicine and preserve the quality of care . . . determined enough that medicine will serve no master except service itself ".

And the best way to maintain a spirited and determined AMA, according to Dr. Parrott, is to give it "a voice which is clear and distinct amid the hubbub of controversy".

Thus Dr. Parrott called for the abolishment of the offices of AMA president, president-elect, vice-president, and immediate past president.

He further urged that the speaker and vice speaker of the House of Delegates be given votes on the Board of Trustees, and that the chairman of the board be elected directly by the House after nomination by the Board.

"Hence", Dr. Parrott said, "the chief leaders—and chief spokesmen—of the AMA would be the board chairman, acting for the elected officers and the House, and the executive vice-president, acting for the staff ".

Such a streamlining would result in a continuum of Association experience and policy, Dr. Parrott said. His recommendations were referred to the Council on Long Range Planning and Development, which is studying a possible reorganization of the AMA.

A reorganization of the AMA at its top level is necessary, Dr. Parrott said, if the Association is to achieve its overriding goal: maintaining the high quality of care.

Final Remarks to the House, Malcolm H. Todd, Outgoing President of AMA

"Future shock" has created an "identity crisis" in American medicine, including the AMA, according to Malcolm C. Todd, AMA president, who gave his final report to the House on Sunday, June 15.

"Future shock", Dr. Todd said, "has hit our Association so abruptly, so hard, and in so many ways, that it has caused an identity crisis. Physicians wonder what the American Medical Association is today."

To remedy that, he suggested that continuity be established between past, present and future so the strengths of tradition could be drawn upon to make the future more solid.

Thus he said physicians must understand that the AMA, in coping with its own future shock, "is not abandoning its historic goals, but merely updating them".

And Dr. Todd urged that the AMA focus substantial energies on "quality of care—the objective for which this association was founded". The major thrust of this effort should be towards education, especially continuing education.

In support of that thrust, he asked delegates to consider AMA establishment of a "university without walls for continuing education".

"Operating in coordination with the medical schools, this university might confer an advance degree after a full year of educational activity. Through its university status and its conferral of degrees, it would lend a new image and a new prestige to continuing education", Dr. Todd said.

Dr. Todd called for a re-emphasis in medical schools on the training of men and women to practice medicine, rather than the growing emphasis on research and the training of researchers.

The National Institutes of Health, he said, are the logical pathways to research, and urged that the AMA legislatively support increased funding and physician involvement in the institutes' advisory bodies.

Several other areas call for decisive political action by the AMA, he said. "Medicine no longer can enjoy the privilege of being a sanctum . . . Politically, a steady stream of legislation—such as PSRO, HMO, public utility type legislation, and health manpower bills—has fallen upon our heads in heavy drops, like the water torture of the ancient Chinese.

"Often more important than the laws, are the highhanded regulations they entail—such as those on utilization review. Without any authorization from the U.S. Constitution, the regulatory agencies have become so powerful that I call them the fourth branch of government".

Thus Dr. Todd said the AMA must be concerned with "Big Brother" government. At the same time, he said, the AMA must support health programs to benefit all the "little brothers in America".

So he concluded that, "This Association must have the full support of our profession—numerically, morally, and financially. Otherwise it cannot do what it has to do, and we, as a profession, cannot do what we have to do".

At the same time, delegates endorsed efforts to increase the $10,000 maximum limit on federally-insured loans to medical students, and to encourage a continuation of federal support for medical and health manpower programs.

In other actions related to Physicians and Hospitals and Medical Schools, the House:

—Adopted two reports addressing provisions for safeguarding medical student records.

—Endorsed AMA support for the drafting of essentials for residency programs in emergency medicine.

—Reaffirmed the AMA position that physician assistants in hospitals should be supervised by physicians, and urged that the policy be widely disseminated.

Miscellaneous Actions of the House

Miscellaneous House actions include:

—Approval of Annual Conventions in St. Louis, 1978; in New York, 1979; in Las Vegas, 1980; in San Francisco, 1981; and in Dallas, 1982.

—Referral for further study and subsequent report model state legislation for the confidentiality of medical records.

—Encouragement of the development of medical-legal symposia involving medical and law students by AMA and ABA representatives.

—Filing of a Board report which assures the House that AMA's anti-quackery activities will be maintained.

—A recommendation that medical schools recognize contributions of women in medicine and promote equal opportunities for them in education and in practice.

—Adoption of a Board report defining planned patient education programs and suggesting they be reimbursable under health insurance.

—A recommendation that all medical students be given opportunities for primary care experiences in inner city or rural areas.

—Support for continued AMA involvement in the evaluation of services to be provided by emerging health occupations, and in judging the appropriateness of each occupation.

John M. Wood, M.D.
Robert E. McCurdy, M.D.
Kenneth A. Platt, M.D.

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Guest Faculty
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John H. Laragh, M.D., Cornell University, New York
Morton H. Maxwell, M.D., University of California, Los Angeles
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For registration and requests for information, contact: Registrar, American College of Physicians, 4200 Pine St., Philadelphia, PA 19104

MEETINGS

American College of Physicians

LABORATORY MEDICINE: CLINICAL APPLICATIONS

Vail Motor Lodge, Vail, Colorado

August 18-21, 1975

Contact: Registrar, Postgraduate Courses, ACP, 4200 Pine Street, Philadelphia, Pennsylvania 19104

Montana-Wyoming Chapter of the American College of Surgeons

ANNUAL MEETING

Sojourner, Teton Village, Jackson, Wyoming

August 23-25, 1975

Contact: Elmer Kobold, MD, 1230 N. 30th, Billings, Montana 59101.

American College of Cardiology

TUTORIALS IN THE TETONS (Cardiac Emergencies)

Jackson Lake Lodge, Moran, Wyoming

August 23-25, 1975

Contact: University of Nebraska Medical Center, Omaha, Nebraska.

University of Colorado School of Medicine, Continuing Medical Education

GYNECOLOGY

Jackson Lake Lodge, Moran, Wyoming

August 18-21, 1975

* * *

PATHOLOGY IN PEDIATRICS

Given Institute of Pathobiology
Aspen, Colorado

August 28-31, 1975

* * *

12TH ANNUAL HOSPITAL MEDICAL STAFF CONFERENCE

Estes Park, Colorado

September 8-12, 1975

* * *

BATTERED CHILD SEMINAR

September 29-30, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

American Society of Anesthesiologists

REGIONAL REFRESHER COURSE

Jackson Lake Lodge, Moran, Wyoming

August 30-31, 1975

Contact: American Society of Anesthesiologists, Inc., 515 Busse Highway, Park Ridge, Illinois 60068.

International Union Against Cancer

SECOND UICC TRAINING COURSE IN CANCER RESEARCH

The Netherlands Cancer Institute,
Sarphatistraat 108,
Amsterdam 1004, The Netherlands

September 7-20, 1975

Fitzsimons Army Medical Center
Pulmonary Disease Service-Allergy-Immunology Service

28TH ANNUAL SYMPOSIUM ON PULMONARY DISEASE

Fitzsimons Army Medical Center, Denver

September 8-12, 1975

Contact: Roald A. Nelson, MD, Fitzsimons Army Medical Center, Denver 80240.

Lovelace Foundation for Medical Education and Research

OUTPATIENT DIAGNOSIS AND MANAGEMENT OF MEDICAL/SURGICAL EMERGENCIES

Lovelace Center for the Health Sciences,
5200 Gibson Boulevard, Albuquerque, New Mexico

September 12-13, 1975

Contact: Office of Medical Education, 5200 Gibson Blvd., SE, Albuquerque, New Mexico 87108, or Call (505) 842-7353.

American College of Physicians
Montana-Wyoming

ANNUAL REGIONAL MEETING

Jackson Lake Lodge, Jackson, Wyoming

September 12-13, 1975

Contact: Allan L. Goulding, MD, P.O. Box 2555, Billings, Montana 59103.

American Cancer Society-
National Cancer Institute

NATIONAL CONFERENCE ON CANCER RESEARCH AND CLINICAL INVESTIGATION

Hyatt Regency Atlanta Hotel, Atlanta, Georgia

September 20-22, 1976

Contact: American Cancer Society, Colorado Division, Inc., 1809 East 18th Avenue, Denver, Colorado 80218, or Call: (303) 321-2464.

American Academy for Cerebral Palsy

29TH ANNUAL MEETING

Fairmont Hotel, New Orleans, Louisiana

September 24-28, 1975

Contact: American Academy for Cerebral Palsy, 1255 New Hampshire Avenue, N.W. Washington, D.C. 20036.

Montrose Memorial Hospital

MONTROSE FALL CLINICS

Elk's Lodge, Montrose, Colorado

September 26-27, 1975

10 hours Credit: AAFP, ACGP

Contact: N. Robert Brethouwer, D.O., Chairman, Fall Clinics Committee, Montrose Memorial Hospital, Montrose, Colorado 81401.

American Burn Association

EARLY MANAGEMENT OF PATIENTS WITH THERMAL INJURIES

Crown Center Hotel, Kansas City, Missouri

September 26-27, 1975

Contact: David Robinson, MD, University of Kansas Medical Center, Kansas City, Kansas.

American Academy of Family Physicians

SCIENTIFIC ASSEMBLY

McCormick Place, Chicago, Illinois

October 6-9, 1975

Contact: American Academy of Family Physicians, 1740 W. 92nd Street, Kansas City, Missouri 64114.

Medical Society of the
United States and Mexico

23RD ANNUAL MEETING

San Francisco, California

October 8-11, 1975

Contact: Mrs. Virginia E. Bryant, 333 West Thomas Road, Suite #207, Phoenix, Arizona 85013.

Montana Medical Association

97TH ANNUAL MEETING

Ramada Inn, Butte, Montana

October 9-11, 1975

American College of Surgeons

61ST ANNUAL CLINICAL CONGRESS

Fairmont Hotel, San Francisco, California

October 13-17, 1975

Contact: American College of Surgeons, 55 East Erie St., Chicago, Illinois 60611.

Albuquerque Cardiovascular Associates, Ltd.

ELECTROCARDIOGRAPHIC INTERPRETATION FOR THE CLINICIAN

**Presbyterian Hospital Center,
Albuquerque, New Mexico**

October 23-25, 1975

Contact: Barry W. Ramo, MD, 201 Cedar S.E., Suite 604, Albuquerque, New Mexico 87106.

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Elective sessions will include: **behavior modification:** obesity, smoking, alcoholism; **bones and joints:** neck and arm pain, low back and leg pain, bursitis and tendonitis, athletic injuries; **medical emergencies:** resuscitation, arrhythmias, drug ingestion, coma; **allergy:** hay fever, asthma, eczema and urticaria; **problem-oriented records:** the defined data base, construction of the problem list, workshop; **trauma:** hand injuries, face injuries, head and spine injuries, chest injuries; **dermatology:** contact dermatitis, bacterial and viral infections, fungal infections, dermatoses; **acid-base:** acidosis, alkalosis, mixed problems; **salt and water problems:** water, sodium, potassium, miscellaneous syndromes.

Faculty for this course will consist of thirty-four physicians of the Stanford University School of Medicine.

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This course will review in detail the current status of management principles and procedures applicable to critically ill and critically injured persons. Topics of general interest will be covered in morning lectures, with the afternoon program offering a choice of problem-solving sessions and seminars and demonstrations in specialized topics. Twenty-nine Stanford University School of Medicine faculty members will participate.

General lectures will cover: hemodynamic monitoring, antiarrhythmic drugs, surgery for ischemic heart disease, respiratory failure: pathophysiology-manifestations and management, the practical use of ventilators, clotting mechanisms, common bleeding problems: congenital-acquired, diabetic ketoacidosis and hyperosmolar coma, lactic acidosis, coma, thromboembolism, drainage of the urinary tract.

Elective sessions will include: **EKG problems:** acute myocardial infarction, tachyarrhythmias, bradyarrhythmias, changes in severe illness; **blood gas and acid-base problems:** respiratory acidosis and alkalosis, metabolic acidosis, metabolic alkalosis, oxygen transport; **salt and water problems:** water, sodium, potassium, miscellaneous syndromes; **acute myocardial infarction:** cardiogenic shock, arrhythmias, emergency surgery, acute rehabilitation in CCU; **ICU methods:** resuscitation, ventilator workshop, central venous pressure and arterial catheters, pacemakers; **trauma:** injuries to the face, injuries to the chest, injuries to the head and spine; **neonatal crises:** neonatal asphyxia, respiratory distress syndrome, sepsis, metabolic crises in the newborn; **ICU management problems:** use of blood components, acute renal failure, antibiotics in septic crises, hyperalimentation.

Tuition for this course is $250 with registration required no later than October 31. Early registration is advisable as this course has been oversubscribed in previous years.

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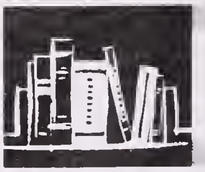

THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Acupuncture Anesthesia: National Institutes of Health, 1975. 339 p. Gift.

Acupuncture Anesthesia in The People's Republic of China: James Y. P. Chen. National Institutes of Health, 1975.

Bonney's Gynaecological Surgery: John Hawkins and Sir John Stallworthy. Williams and Wilkins, 1974. 868 p. $37.75.

Cerebrovascular Disease: James F. Toole and Aneel N. Patel. 2nd ed. McGraw-Hill, 1975. 412 p. $17.50.

Clinical Biochemistry: Albert L. Latner. 7th ed. Saunders, 1975. 918 p.

Combination Drugs; Their use and Regulation: Louis Lasagna, ed. Intercontinental Medical Book Corporation, 1975. 186 p. $15.00.

Comprehensive Textbook of Psychiatry: Alfred M. Freedman, Harold I. Kaplan, and Benjamin J. Sadock. 2nd ed. Williams and Wilkins, 1975. 2 v. $65.00.

Diccionario Ingles-Espanol. Editorial Alhambra, 1973. 713 p. $20.00.

Drug Interactions: P. L. Morselli, S. Garattini and S. N. Cohen, ed. Raven Press, 1974. 406 p. (Monographs of the Mario Negri Institute for Pharmacological Research) $28.00.

French-English Science Dictionary: Louis DeVries. 3rd ed. New York, McGraw-Hill, 1968. 655 p. $12.50.

Gastroenterology: Henry L. Bockus, ed. 3rd ed. Saunders, 1974. v. 1. $35.00.

Genetic Screening; Programs, Principles, and Research: National Research Council. Committee for the Study of Inborn Errors of Metabolism. National Academy of Sciences, 1975. 388 p. Gift.

Gross Pathology, A Color Atlas: R. C. Curran and E. L. Jones. Oxford University Press, 1974. 147 p. $19.50.

Handbook of Ocular Pharmacology: Marvin Smith. Publishing Sciences Group, 1974. 156 p. $11.25.

Health Organizations of the United States, Canada, and Internationally; A Directory of Voluntary Associations, Professional Societies and other Groups Concerned with Health and Related Fields: Paul Wasserman and Joan Giesecke, eds. McGrath Publishing Co., 1974 3d ed. 249 p. $24.00.

Human Poisoning from Native and Cultivated Plants: James W. Hardin. Duke University Press, 1974. 194 p. $6.75.

Immunology in Medical Practice: Geoffrey Taylor, ed. Saunders, 1975. 396 p. $13.50.

Inflammatory Bowel Disease: Joseph B. Kirsner and Roy G. Shorter, eds. Lea & Febiger, 1975. 465 p. $32.50.

Major's Physical Diagnosis: Mallon Delp and Robert Manning, eds. 8th ed. Saunders, 1975. 790 p. $15.75.

Malformation Syndromes: Daniel Bergsma, ed. (Boston Conference on the Diagnosis, Genetics and Management of Birth Defects, 1974) Intercontinental Medical Book Corporation, 1974. 200 p. (Birth defects; original article series, v. 10, no. 7) $12.95.

Manual of Dermatologic Therapeutics: Kenneth A. Arndt. Little, Brown and Company, 1974. 290 p. $8.95.

The Manufacture of Madness, A Comparative Study of the Inquisition and the Mental Health Movement: Thomas S. Szasz. Harper and Row, 1970. 383 p. $9.95.

Medical Aspects of Drug Abuse: Ralph W. Richter, ed. Harper and Row, 1975. 399 p. $22.50.

Medical Oncology: K. D. Bagshawe, ed. Blackwell, 1975. 588 p. $52.50.

Minimal Brain Dysfunction: Mortimer D. Gross and William C. Wilson. Brunner/Mazel, 1974. 206 p. $10.95.

Modern Drug Encyclopedia and Therapeutic Index: Arthur J. Lewis. 13th ed. Donnelley, 1975. 922 p. $29.00.

National Physician Assistant Program Profile, 1975-1976: Association of Physician Assistant Programs, 1974. 126 p. $3.00.

Occupational Lung Diseases: William K. Morgan and Anthony Seaton. Saunders, 1975. 391 p. $16.20.

Physical Examination of the Surgical Patient: John E. Dunphy and Thomas W. Botsford. 4th ed. Saunders, 1975. 414 p. $16.00.

Plastic Surgery, New Methods and Refinements: Tord Skoog. Saunders, 1974. 500 p. $120.00.

Principles of Bacteriology, Virology, and Immunity: Graham S. Wilson and A. A. Miles. 6th ed. Williams and Wilkins, 1975. 2 v.

Principles of Drug Action: The Basis of Pharmacology. 2d ed. Wiley, 1974. 854 p. $21.50.

Symposium on Cell Patterning. Elsevier, 1975. 356 p. (Ciba Foundation symposium, 29) Gift.

Symposium on the Structure and Function of Chromatin. Elsevier, 1975. 368 p. (Ciba Foundation symposium, 28) Gift.

Textbook of Medicine: Paul B. Beeson and Walsh McDermott, eds. 14th ed. Saunders, 1975. 1892 p. $32.00.

The Uncertain Miracle, Hyperbaric Oxygenation: Vance Trimble. Doubleday, 1974. 236 p. $6.95.

Use of Medical Literature: Leslie T. Morton, ed. Butterworth, 1974. 406 p. $20.00.

The Denver Medical Society and its staff would like to thank the Colorado Otolaryngological Society for its recent gift of the 1976 subscription of Laryngoscope. We are happy to see the society taking an interest in the library.

Also, a note of thanks to Mrs. Bertram Pear for her recent gift of her drawing which is on display in the library.

OBITUARIES

Montana

Phillip E. Griffin, Sr., MD, 75, died at Deaconness Hospital in Billings, Montana of a heart condition on Sunday, May 11.

He was born in Diamondville, Wyoming May 29, 1899, and attended school in Roundup. He was a graduate of the University of Montana. He attended medical school at the University of Minnesota, and interned in Seattle. He was a veteran of World War I.

In 1932 Dr. Griffin came to Billings to associate with Dr. Louis Allard at the Allard Clinic. In 1945 he opened his own practice in the Hart Albin Building where he continued to practice up to the time of his death.

Dr. Griffin served many years as physician for School District No. 2. He belonged to the Yellowstone Valley Medical Society, which he served as president for two terms, as well as to the American Medical Association.

He was married to Erna Hummel in 1946. She survives, as do two sons, Dr. Phillip E. Griffin, Jr., and George Griffin, both of Billings, two daughters, Marjorie Griffin of Tacoma, Washington, and Mrs. Carolyn Richard, Bellingham, Washington. Two brothers, Harry P. Griffin of Sheridan, Wyoming, and Walter Griffin of Missoula survive, as do four sisters, Mrs. Bess Quinton, Anchorage, Alaska, Mrs. Ruth Cox, LaSalle, Illinois, Mrs. Dorothy Watts, Minneapolis, Minnesota, and Mrs. Molly Britton, Lakewood, New Jersey, and five grandchildren.

Colorado

Maurice Chernyk, MD, died May 20, 1975. Though he had been in ill health for some time, he continued to practice due to the insistence of his patients.

He was born March 23, 1903 in Russia, his family moving to the United States in 1910, and settling in Waterloo, Iowa. Later they moved to Del Norte, Colorado, where the elder Mr. Chernyk managed a ranch. Subsequently they moved to Denver, and Maurice attended North Denver High School.

After graduation he attended the University of Denver, then the University of Colorado School of Medicine. He first practiced in Frederick, Colorado, then came to the National Jewish Hospital to become associated with Dr. Leon Bronfin, and acquired his skill as a thoracic surgeon. He was on the active staffs of both General Rose Memorial and Beth Israel hospitals, having served as chief of staff of the latter.

Last February Dr. Chernyk received the Distinguished Service Award from Beth Israel, having served on its staff for over 50 years. In October 1974 he was honored by the Denver Medical Society for his long years of service. He had never married, and made his home with his brother Sam and two sisters, Nellie Chernyk and Mrs. Hazel Brown, all of whom survive the doctor.

Selvie J. Curtis, MD, died May 24, 1975 at the Swedish Medical Center in Englewood, Colorado, after a short illness. Born in Tennessee, October 30, 1903, he received his MD from the University of Oklahoma in 1928, and joined the U.S. Army for his graduate training and a subsequent career.

He was at one time Chief of Medical Services at Fitzsimons General Hospital. He retired from the Army in 1947 as a Colonel, and opened a private practice in Denver, which he maintained until his death.

He was a member of the Denver and Colorado Medical Societies, and the American Medical Association. He belonged to the American Academy of Family Physicians and was on the staff of St. Luke's Hospital.

A widower, Doctor Curtis was married to Lois M. Edison in Cheyenne, Wyoming in 1968, and she survives him. Also surviving are a son Mark Edison; a sister, Mrs. Etta Hinton of Altus, Oklahoma, and a brother, V. L. Curtis of Oklahoma City.

Merritt G. Ringer, MD, Longmont, Colorado, died Sunday, June 22, 1975, after a long illness. He was born December 24, 1899 in Chicago, Illinois. He attended Kenyon College, Gambier, Ohio, then received his MD from Northwestern University, Evanston, Illinois, in 1925. He joined the U.S. Army Medical Corps upon graduation, and received all his graduate education in the service.

In 1937 he was certified by the American Board of Otolaryngology. During World War II he commanded a field hospital in North Africa. At the time of his retirement from the Army in 1948 he was head of the Otolaryngology Department at Walter Reed Hospital, Washington, D.C.

In 1949 he became associated with the Longmont Medical Clinic, practicing his specialty of ear, nose, and throat.

His wife, Alice Neilson Ringer, died in 1970, and in 1971 he was married to Evelyn Seedle, Longmont. He belonged to the Boulder County and Colorado Medical societies, and the American Medical Association. He belonged to the American Academy of Ophthalmology and Otolaryngology. He was a Mason, belonged to the Shrine, Rotary Club, and Elks Lodge.

He is survived by his wife, a son, Merritt G. Ringer, Jr. MD, Boulder; a stepson, Major Don Seedle, Alameda, California; a stepdaughter, Mrs. Sue Branch, Golden, Colorado, and three grandchildren.

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Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)

Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy.
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Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines. Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.
PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi, discontinue antibiotic and start appropriate therapy.

In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.

Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.

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Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner, Food and Drug Administration

The idea of a so-called patient package insert has been around fo a long time. Many physicians alread use written instruction sheets to provide patients with information about the drugs they are taking. An some physicians give verbal instruc tions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit wit glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and there fore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as a extension of drug labeling.

The benefits of patient involvement

Many physicians may not real ize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. An this information is almost always bad or irrelevant to the case at han Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impresse by the principle that the best way to get someone to do something is to involve him in the process. So the

---

Dr. James H. Sammons
Executive Vice President of the American Medical Association

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

main purpose of drug information for the patient is to get his coopera-on in following a drug regimen.

Preparation and distribution of atient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administra-ion. There is nothing wrong with his agency saying, "this informa-ion is generally agreed upon and herefore it should be used," as long is our process for getting the information is sound.

Distribution of the information s a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting proges-erone, we would think it mandatory o issue two separate leaflets—a short one for the patient to read be-ore getting the first shot and a long one to take home in order to make a decision about continuing therapy. n this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this nformation might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the nsert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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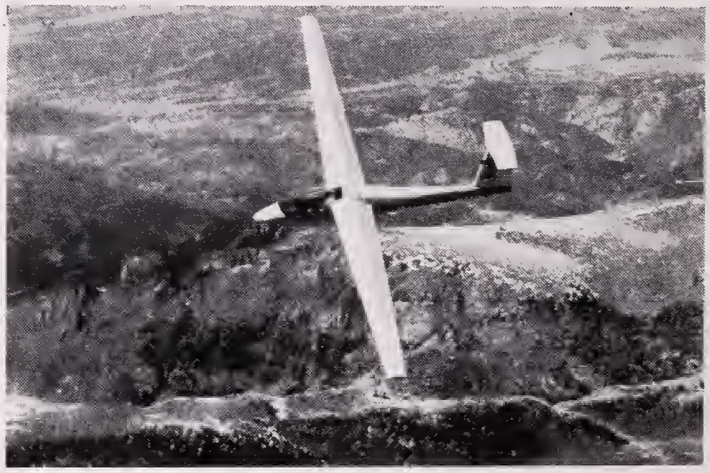

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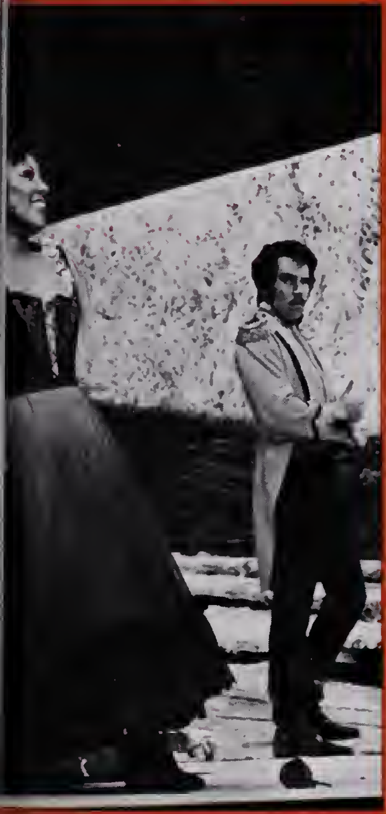
September 1975

VOLUME 72 • NUMBER 9



Both often

Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequenc and/or severity of grand mal seizures ma require increased dosage of standard ant convulsant medication; abrupt withdrawa may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuanc (convulsions, tremor, abdominal and mus cle cramps, vomiting and sweating). Kee addiction-prone individuals under careful

respond to one

According to her major
ymptoms, she is a psychoneu-
otic patient with severe
nxiety. But according to the
lescription she gives of her
eelings, part of the problem
nay sound like depression.
This is because her problem,
although primarily one of ex-
essive anxiety, is often accom-
anied by depressive symptom-
tology. Valium (diazepam)
an provide relief for both—as
he excessive anxiety is re-
ieved, the depressive symp-
oms associated with it are also
often relieved.

There are other advan-
tages in using Valium for the
management of psychoneu-
rotic anxiety with secondary
depressive symptoms: the
psychotherapeutic effect of
Valium is pronounced and
rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium®
(diazepam)
2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Roche Laboratories
Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

ROCKY MOUNTAIN MEDICAL JOURNAL

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SEPTEMBER 1975

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OUR COVER

New Mexico's most prized cultural ornament is the Santa Fe Opera in the sage-hrushed hills above Tesuque, outside Santa Fe. Each summer since 1957 it has offered what *The New Yorker's* Winthrop Sargeant has called "the most sophisticated opera to he seen and heard in America". Productions are in the 1700-seat theatre built in 1968 to replace the original smaller one which burned down in 1967. Scenes from two popular operas are blended into the cover montage. At top are scenes from Ravel's fantasy, "The Child and the Sorcerers", and below are glimpses of Bizet's "Carmen". Through the open portals at the rear of the stage in the very bottom picture can be seen the Jemez Mountains in which Los Alamos nestles, and whose lights have served as those of Nagasaki. Credit: Ken Howard, 1975 Santa Fe Opera.

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*Higgs, R. H., Smyth, R. D., and Castell, D. O., Gastric Alkalinization—Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin, *The New Engl. J. of Med.*, 291, 486-490, 1974.

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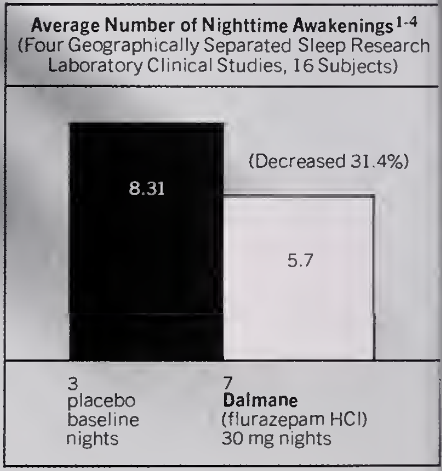

Average Number of Nighttime Awakenings[1-4]
(Four Geographically Separated Sleep Research Laboratory Clinical Studies, 16 Subjects)

And for those with trouble alling asleep or sleeping ong enough…

…Dalmane (flurazepam HCl) lso delivers excellent results. Clinically proven in sleep research laboratory studies: on average, leep within 17 minutes that lasts 7 to 8 hours.[5]

Dalmane (flurazepam HCl) s relatively safe, seldom causes morning "hang-over."..

…and is well tolerated. The usual adult dosage is 30 mg *h.s.*, but with elderly and debilitated patients, limit the initial dose to 15 mg to preclude oversedation, dizziness or ataxia. Evaluation of possible risks is advised before prescribing.

REFERENCES:

1. Karacan I, Williams RL, Smith JR: The sleep laboratory in the investigation of sleep and sleep disturbances. Scientific exhibit at the 124th annual meeting of the American Psychiatric Association, Washington DC, May 3-7, 1971
2. Frost JD Jr: A system for automatically analyzing sleep. Scientific exhibit at the 24th annual Clinical Convention of the American Medical Association, Boston, Nov 29-Dec 2, 1970; and at the 42nd annual scientific meeting of the Aerospace Medical Association, Houston, Apr 26-29, 1971
3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

Dosage: Individualize for maximum beneficial effect. *Adults:* 30 mg usual dosage; 15 mg may suffice in some patients. *Elderly or debilitated patients:* 15 mg initially until response is determined.

Supplied: Capsules containing 15 mg or 30 mg flurazepam HCl.

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(flurazepam HCl)

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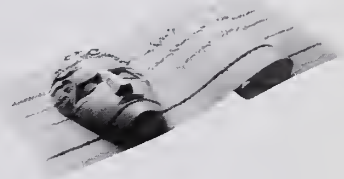
One 15-mg capsule *h.s.*— initial dosage for elderly or debilitated patients.



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1. Dermatology for Non-Dermatologists
2. Evaluation of the Unconscious Patient
3. Hyperlipidemia
4. Infectious Diseases in Children
5. Management of Adolescent Problems
6. Newer Antibiotics
7. Newer Concepts of Family Planning
8. Office Management of Sexual Difficulties
9. Peripheral Vascular Disease—Diagnosis and Treatment
10. Pulmonary Function Tests and Blood Gases

Monday-Wednesday, Dec. 1-3 (Numbers 1-10)
1st Choice # ____; 2nd Choice # ____; 3rd Choice # ____

Monday-Wednesday, Dec. 1-3/10:30 AM-Noon (4½ hour, 3-day course: $45)

11. Acid-Base, Fluid and Electrolyte Balance
12. Advanced Electrocardiography
13. Critical Patients—Critical Decisions
14. Normal and Abnormal Uterine Bleeding
15. Office Management of Anorectal Disorders
16. Office Practice of Gynecology
17. Physicians' Marriages
18. Special Problems of Child Abuse
19. Surgical Lesions of the Intestines—Diagnosis and Treatment
20. Treatment of Common Pediatric Allergies

Monday-Wednesday, Dec. 1-3 (Numbers 11-20)
1st Choice # ____; 2nd Choice # ____; 3rd Choice # ____

Thursday-Friday, Dec. 4-5/7:30-10:30 AM (6 hours for total course; 3 hours on Thursday, 3 hours on Friday: $60)

21. Acid-Base, Fluid and Electrolyte Balance (repeat)
22. Basic Electrocardiography
23. Birth Defects and Clinical Genetics
24. Dermatology for Non-Dermatologists (repeat)
25. Fetal Monitoring
26. Ophthalmoscopy for the Non-Ophthalmologist
27. Pediatric Cardiology
28. Pitfalls of Emergency Room X-Rays
29. Office Endocrinology
30. Immunology—1976
31. The Uterine Pap Smear

Thursday-Friday, Dec. 4-5 (Numbers 21-31)
1st Choice # ____; 2nd Choice # ____; 3rd Choice # ____

Offered Both Monday & Tuesday, Dec. 1 & 2 /7:30 AM-Noon (4½-hour course: $45)

32. Basic Life Support—Cardiopulmonary Resuscitation (Dec. 1) ____
33. Basic Life Support—Cardiopulmonary Resuscitation (Dec. 2) ____

Wednesday-Friday, Dec. 3-5/9:00 AM-Noon (9-hour course: $90)

34. Advanced Life Support—Cardiopulmonary Resuscitation. (Prerequisite: Basic Life Support Course) (Dec. 3-5) ____

Courses of the AMA Committee on the Medical Aspects of Sports (Each a 3-hour course: $30)

Monday, Dec. 1/7:30-9:00 AM & 10:30-Noon
35. The Physical Exam ____

Tuesday, Dec. 2/7:30-9:00 AM & 10:30-Noon
36. The Oriental Arts (Karate, Judo, Yoga) ____

Wednesday, Dec. 3/7:30-9:00 AM & 10:30-Noon
37. Emergency Care on the Field ____

Thursday, Dec. 4/7:30-10:30 AM
38. Wrestling ____
39. Aquatic Sports ____

Friday, Dec. 5/7:30-10:30 AM
40. Rehabilitation ____

Tuesday-Wednesday, Dec. 2-3/7:30-10:30 AM (6 hours for total course; 3 hours on Tuesday, 3 hours on Wednesday: $60)
41. Writing for Scientific Journals ____

LUNCHEON ROUND TABLES

(Held in Hilton Hawaiian Village Long House Room, luncheon round tables are jointly sponsored by the AMA Auxiliary and AMA Council on Scientific Assembly. Cost: $10.00 each.)

Tuesday, December 2 (12:15-1:45 PM) • Topic—Ancient Polynesian Medicine ____

Thursday, December 4 (12:15-1:45 PM) • Topic—Dehli Belly, Gyppy-Tummy, and Other Diseases of Travelers ____

General Registration

____ Non-member physicians: $35
____ Guests of non-members: $10
____ Foreign M.D.'s: no fee
____ AMA members and their guests: no fee
____ Medical students, interns and residents: no fee

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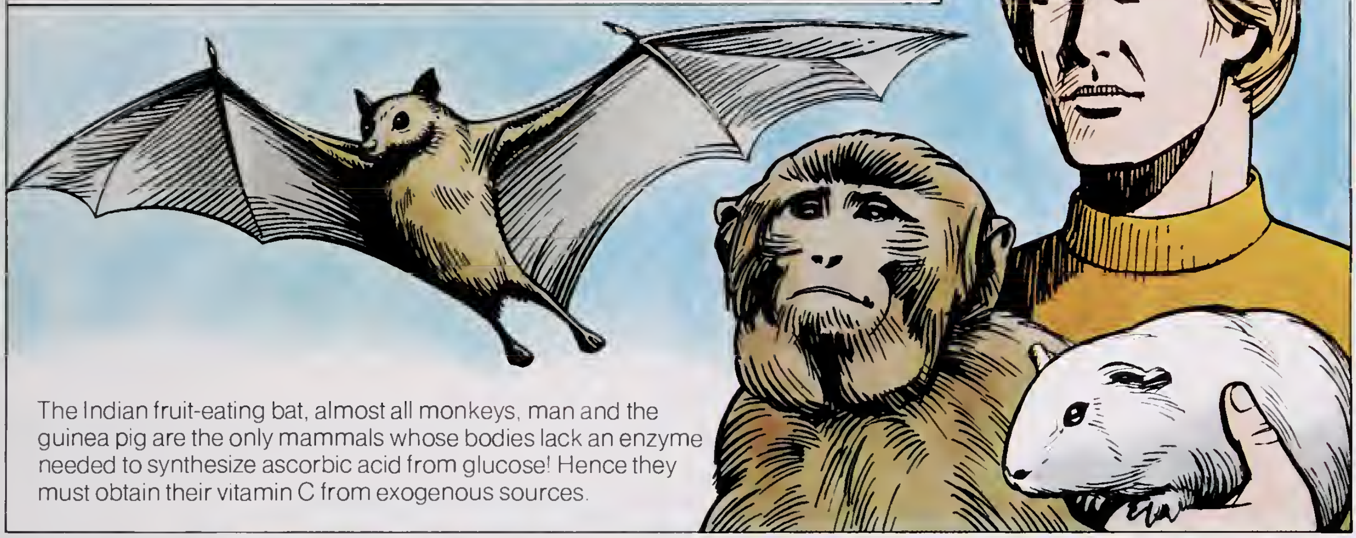
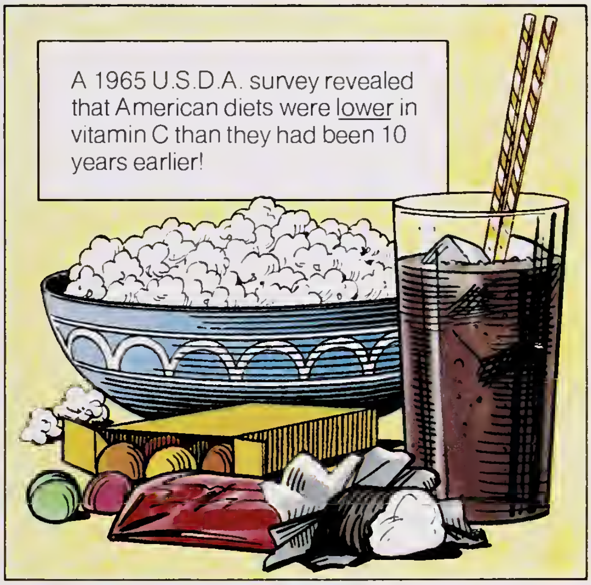


The Indian fruit-eating bat, almost all monkeys, man and the guinea pig are the only mammals whose bodies lack an enzyme needed to synthesize ascorbic acid from glucose! Hence they must obtain their vitamin C from exogenous sources.

De Joinville writing about a 13th century crusade reported that barber surgeons had to "cut away the dead flesh from the gums to enable people to masticate their food." The disease he described was probably scurvy.

A 1965 U.S.D.A. survey revealed that American diets were lower in vitamin C than they had been 10 years earlier!



The outer leaves of cabbage and brussels sprouts contain more vitamin C than the heads. Yet, ironically, these are often trimmed away by the grocer to improve appearance and enhance sales appeal! Many housewives trim them even more before cooking!

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hyoscine hydrobromide	0.0065 mg	0.0065 mg	0.0195 mg.
phenobarbital	(¼ gr.) 16.2 mg	(½ gr.) 32.4 mg.	(¾ gr.) 48.6 mg
(warning: may be habit forming)			

Brief summary. Adverse Reactions: Blurring of vision, dry mouth, difficult urination, and flushing or dryness of the skin may occur on higher dosage levels, rarely on usual dosage. Contraindications: Glaucoma: renal or hepatic disease; obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); or hypersensitivity to any of the ingredients.

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Malpractice and Scapegoatism

The value of a human has increased. In frontier days it could not have been much, judging from the forty notches on Wild Bill Hickok's gun. During World War II, a dead GI was worth $10,000, the sum paid to his beneficiary by National Service Life Insurance. In the fine print on my airline ticket the liability of certain airlines for personal injury or death is limited by the Warsaw Convention to no more than $75,000 per passenger, or if legal fees are not included, to $58,000, or under certain circumstances (if the carrier had not signed the agreement, or had no agreed landing area in the U.S.) to $10,000.

When one compares these amounts and others established by workmen's compensation panels and insurance companies for loss of limb, sight, disability, or death, with the multimillion dollar malpractice awards, one realizes why physicians, hospitals, drug houses and insurance companies are in grave jeopardy. Disaster lurks in every scalpel, every syringe, every capsule . . . in an unforeseen mishap, a poor result, an error.

Years ago in collected data from all over the world I discovered that the extent of error in clinical practice, determined by verifying the clinical diagnosis by the postmortem examination, ranged from six to fifty-seven per cent, and in diagnostic procedures from four to sixty per cent. Errors occur in all human activities. Consider the divorce rate. Computers make mistakes, and it has been suggested that in critical matters data should be fed into three general purpose computers, and if two agree, the answer from the third disagreeing computer should be discarded. Particularly appropriate is a report showing that thirty-four per cent of patients' statements as to their circumcision status were in disagreement with physical findings.

Because physicians deal daily with people's lives, efforts should be made to ensure that our performance is at a high level. It is difficult to understand why we are more severely punished than others who also deal in matters of life and death when found guilty of negligence or poor judgment. In a local case, a woman was accidentally shot to death by a policeman in the performance of his duty; an out-of-court settlement for $14,000 was greeted happily by the lawyer for the dead woman's family. A few months ago sixteen people died in an aircraft disaster. Inquiry showed that a traffic controller in Seattle had ordered the pilot to maintain a five thousand foot altitude, at which level he crashed into a mountain. The order was intended for a different plane. "It was human error", said the Federal Aviation Administration director. The possibility of a jury foreman making such an announcement following the trial of a surgeon for amputating the wrong leg is incomprehensible.

There is other evidence of inequity in the treatment of physicians. Often judgments are rendered against us because of poor results ("the result speaks for itself") despite agreement that the physician did nothing wrong. Twenty-two years ago a premature infant was placed in an incubator in a highly saturated oxygen atmosphere, an accepted treatment at that time. She became blind. Later, the disease which caused the blindness, retrolental fibroplasia, was traced to the use of oxygen. Three years ago a suit was instituted and this year the verdict was announced — two physicians and the hospital guilty of malpractice.

We live in a time when one subject polarizes people, monopolizes their attention, frays their emotions. The day before yesterday it was Vietnam. Yesterday Watergate. Today Malpractice. Everyone tells us what brought about the crisis: doctors keeping patients waiting, making too much money, asking patients to sign consent forms, dehumanization of hospitals, public belief in physician infallibility and medical miracles (the "Dr. Welby Syndrome"), bleeding heart juries convinced that insurance companies and physicians can indefinitely survive six and seven figure awards, the physician shortage, the rise of consumerism, the contingency fee system, no-fault automobile insurance . . .

I think there are two additional reasons.

One, the love of money — the root of all evil.

Awards continue to increase astronomically. None of this has occurred in other countries, suggesting that it is an American phenomenon. Has the vision of sudden wealth replaced the American dream? Are the opportunities to rise from rags to riches now to be found in courtrooms rather than oil fields or the stock market? What does a French baker, a Swedish fisherman, a Canadian farmer, a Chinese factory worker, a Mexican migrant worker, or an Arab merchant think when he hears that the life of an American is worth four million dollars — or a beggar in India watching his child die of starvation — or, for that matter, a Navajo sheepherder?

Two, there is the scapegoat phenomenon. When people cannot express their hostilities because it would bring them into conflict with a miserly boss, a thoughtless spouse, or a repressive government, the inexorable psychologic mechanisms of displacement and projection are set in motion. An outlet needs to be found — hostilities cannot be bottled up. Someone must feel the pressure: a child or wife to abuse, a dog to kick, a minority group to attack. Sometimes the price of scapegoatism is too high, as it was in Nazi Germany.

Physicians are today's scapegoats. No one has been able to solve the problems — perhaps they are insoluble — of our violence-prone, politically corrupt, wasteful, materialistic, anti-intellectual, anti-professional technologic society. We are threatened with depletion of our resources, welfare statism, inflation, unemployment, insensate bureaucratism, global pollution, and mass destruction. Our crime-ridden cities are on the brink of bankruptcy. The public, frustrated, impotent, and without direction, needs to blame someone, and who remains now that members of emergent minorities — Indians, blacks, Jews, Catholics, women — are recognized as also human? Who remains? The medical profession.

For more than a quarter of a century we have been under attack. "AMA" has become a dirty word. Everywhere there are the horror stories, about bungling and incompetent physicians, ghost surgeons, greedy abusers of Medicare and Medicaid, and unnecessary surgery. Our "traditional" method of medical care is said to be disorganized, fragmented, and episodic. We are compared to a corner druggist, neighborhood grocer, or pushcart peddler — all obsolete. Our fee-for-service type of payment has been compared to a pay toilet in a hotel (in a speech printed in an HEW publication). Ours is said to be a "sickness system . . . The more illnesses they (doctors and hospitals) treat and the more services they render — the more their income rises . . ." (from the White Paper of 1971). There are prejudiced T.V. programs like "Don't get sick in America." The social planners, administrators, consumer advocates, HMO advocates, state and federal controllers (FDA, HEW, PSRO), and our own examiners and educators tell us about the heaven of the new health care delivery systems, forgetting that perfection is achieved only in an institution higher than any of ours.

It is obvious that a solution to the crisis must soon be found, one that provides fairly for patients damaged by medical care regardless of the cause of the damage, just as workmen's compensation does for workmen and the government for injured veterans. Sometimes there is human error. Sometimes someone receives a dishonorable discharge. But for the most part, those who fight for the lives of their patients are well-trained, ethical, conscientious men and women dedicated to their service profession.

My feeling of persecution persists. I prefer to believe that we are scapegoats rather than consider the possibility of paranoia. I have joined the doomsters, the black-robed men who feel that our scientific environment has been poisoned by the planners, the bureaucrats, and the mystics. The practice of medicine — an art and a science — had its birth in antiquity, its childhood in the centuries just prior to and following the birth of Christ, its maturity during the scientific revolution, and, I fear, its zenith in the mid-twentieth century.

Marcus J. Smith, MD, Santa Fe

Error

In the article "Clindamycin in Deep Pharyngeal Infections" by G. L. Smith, MD, in the July issue, there is an error in the last sentence on page 298. The phrase "After intravenous clindamycin was started" should be deleted. The response in 48 hours to other antibiotics in this second patient is compared to the response in four hours of the patient who received clindamycin.

Editor

Gonococcal perihepatitis[*]

Presenting as blunt abdominal trauma

**Paul R. Whitwam, MD, C. M. Rippberger, MS,
and Jerry M. Shuck, MD, Albuquerque**

GONOCOCCAL PERIHEPATITIS was first described by Carlos Stejane in 1919,[1] but it was not until 1930 and 1934 when Curtis[2] and Fitz-Hugh[3] respectively published their observations regarding the syndrome, which bears their names. In the next twenty years, several more cases were described and the syndrome was further defined.[4] These early papers emphasized that gonococcal perihepatitis should be part of the differential diagnosis of right upper quadrant abdominal pain, which included cholecystitis, appendicitis, and other more common entities. Nonetheless, many physicians are unacquainted with the Fitz-Hugh-Curtis Syndrome and many others think of it only as a rare complication of gonococcal infection.

As a result of two cases encountered at the Bernalillo County Medical Center, it is now recommended that this syndrome should be considered when evaluating abdominal pain even if the history is clouded by possible blunt abdominal trauma. The continued rise in the number of gonococcal infections throughout the world makes the chances of encountering this entity correspondingly greater.[8]

CASE REPORTS

Case 1. A 19-year-old white woman came to the Emergency Room with a 24 hour history of intermittent, sharp, right upper quadrant abdominal pain which increased with respirations. There was no associated nausea or vomiting and she had noted no change in her bowel habits. She was taking birth control pills. Her last normal menstrual period began 13 days previously. The patient denied exposure to venereal disease. She had had frequent intercourse with the same man for nine months. Her temperature was 37.7 C. orally. Examination showed the lungs to be clear. Palpation of the abdomen disclosed tenderness without rebound just inferior to the right costal margin. The abdomen was otherwise unremarkable. Bowel sounds were hypoactive. The pelvis was normal.

Roentgenograms of the chest and abdomen showed no abnormalities. Catheterized urinalysis was unrevealing and there was no growth on culture. Leukocytosis of 15,200 with 77% neutrophils and 9% bands was present. The patient was admitted with provisional diagnoses which included cholecystitis and rectrocecal appendicitis. Intravenous fluids were started and a nasogastric tube was placed. The pain only partially resolved, yet the white count returned to normal. Gynecologic consultation was obtained and the pelvis was again normal by examination. Oral cholecystography showed non-visualization of the gallbladder, but repeat examination showed a normal gallbladder without calculi.

Further questioning revealed that two weeks prior to admission, the patient had taken her first parachute jump and the possibility was then raised of hepatic trauma. A liver scan disclosed a defect in the right lobe. A fall in hemoglobin from 14.6 Gm% on admission to 12.8 Gm% on her seventh hospital day further increased the possibility of liver injury with subcapsular hematoma. Her condition stabilized, however, there was no change in the scan defect and the hemoglobin remained the same. After two weeks of observation she began to develop right adnexal pain in addition to the mild right upper quadrant abdominal pain. A repeat gynecologic examination showed cul-de-sac fullness. An examination under anesthesia and colpotomy confirmed the diagnosis of acute gonococcal salpingitis and bilateral tubo-ovarian abscesses. In view of the patient's penicillin allergy, intravenous tetracycline was begun with decrease in the size of her tubo-ovarian abscesses and resolution of her right upper quadrant abdominal pain. The defect on liver scan was not explained, and the patient was lost to followup making further evaluation impossible.

Case 2. Four days before admission to the Bernalillo County Medical Center, a 15-year-old girl was thrown from a horse striking the lower lateral portion of her chest against a rock. One day prior to being seen, she developed moderate, continuous, right upper quadrant abdominal pain which was referred to the right shoulder and was more severe with respiration. She had anorexia but had been having normal bowel movements.

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Past history showed that she had frequent indigestion but no fatty food intolerance. She had had intercourse two times in the recent past. Her last menstrual period was normal and occurred ten days before admission. Vaginitis had been present for three months.

The patient was afebrile. Examination of the chest, lungs, and back was unremarkable. Examination of the abdomen showed tenderness to palpation in the right upper quadrant. There was no rebound tenderness. The remainder of the abdomen was soft. Bowel sounds were hypoactive. Pelvic examination showed minimal cervical tenderness and a purulent discharge in the vagina.

Laboratory workup included chest and abdominal x-rays which were unremarkable. Her urine contained 25-30 WBC per high power field. Repeat urinalysis after catheterization was normal with no growth on urine culture. The blood showed 13,500 WBC with 72 neutrophils and 2 bands. The hemoglobin was 13.2 Gm%.

The patient was admitted to the hospital for observation. The differential diagnoses included hepatic laceration, subcapsular hematoma, cholecystitis, and gonorrhea with Fitz-Hugh-Curtis Syndrome. On the first hospital day her abdomen was less tender. The WBC decreased to 7,600 with 51 polys and 0 bands. Normal liver function studies were obtained. However, her sedimentation rate was elevated to 48. The gallbladder visualized poorly on the first oral cholecystogram, but visualized well on repeat study; calculi were not demonstrated. Endocervical culture which had been obtained at the time of admission was positive for *Neisseria gonorrhea.* The diagnosis of Fitz-Hugh-Curtis Syndrome was then made. Intravenous aqueous penicillin resulted in resolution of her pain within two days. She has been followed in the gynecology clinic for nine months with no further problems.

Discussion

Gonococcal perihepatitis is basically a type of peritonitis. At the laparotomy of a patient whose symptoms had recently subsided, Fitz-Hugh observed that a "localized fairly dry peritonitis involved the anterior surface and edge of the liver and the adjacent peritoneal surface of the diaphragm and the anterior abdominal wall. The peritoneum in these areas was injected and had the appearance of salt sprinkled on a moist surface".[3] In his original article, Curtis[2] noted the frequent occurrence of "violin string" adhesions between the liver and abdominal wall in women with pelvic inflammatory disease. Apparently the acute inflammatory reaction described by Fitz-Hugh results in these "violin string" adhesions.[4] The route of spread of the infection is uncertain. It was originally thought to follow the pericolic gutters, but in view of two cases reported in males, it seems reasonable to assume that the infection may also spread via hematogenous or lymphatic routes.[7,11]

Malcolm Stanley published a comprehensive review of the Fitz-Hugh-Curtis Syndrome in 1946.[4] He pointed out that trauma to inflamed pelvic organs in the form of surgical procedures, gynecologic procedures, intercourse, or douching might precipitate the development of gonococcal perihepatitis. In view of the two new cases presented in this manuscript, it seems possible that blunt abdominal trauma may also be a precipitating factor. One previously reported case was thought to be from blunt trauma.[9] However, it is equally possible that the association between the abdominal trauma and the onset of symptoms is no more than temporal.

The Fitz-Hugh-Curtis Syndrome is most often seen in women between 15 and 45 years of age, corresponding to the age group with the highest incidence of gonorrhea. However, cases of gonococcal peritonitis have been described in prepubescent girls.[6,9] Gonococcal perihepatitis may develop immediately or several years after an apparent or inapparent gonococcal infection. Symptoms of perihepatitis may even seem to precede pelvic aspects of the disease.[4] However, gonorrhea is so often asymptomatic in women that it is frequently not considered in patients with striking abdominal symptoms.

The pain of perihepatitis is characteristically localized in the right upper quadrant, although it may begin on the left or bilaterally. Occasionally it is worse in the back. The pain is sharp and sudden in onset. It is exacerbated by deep breathing, coughing, and movement. It may be referred to the shoulder. There may or may not be concurrent pelvic pain. Nausea is a frequent complaint; vomiting somewhat less common. Chills, fever, sweats, and headache are frequently present.

The physical examination is highly variable. It may show an acutely ill person with a moderately elevated temperature. There is tenderness and guarding in the right upper quadrant. Fitz-Hugh originally described a friction rub over the liver similar to the "crunching of new snow",[3] but this sign is usually absent. There may be other signs of gonococcal infection such as vaginal discharge, arthritis, keratosis, blennorrhagia, or skin lesions.

Routine laboratory data are rarely helpful. The white cell count is elevated although usually does not exceed 15,000. Erythrocyte sedimentation rate is high. Abdominal roentgenograms are unremarkable. Chest x-rays show no abnormality except for occasional elevation of the diaphragm on the affected side. Gallbladder series show variable filling but are unreliable. It may be possible to grow *Neisseria gonorrhea* from the urogenital tract or bloodstream. Kimball and Knee were able to obtain a positive culture from a liver biopsy.[7] A positive culture is obviously helpful.

The differential diagnosis of right upper quadrant abdominal pain includes cholecystitis, hepatitis, appendicitis, pancreatitis, acute pyelonephritis, nephrolithiasis, perforated peptic ulcer, subphrenic abscess, and in trauma cases, subcapsular hepatic hematoma and ruptured abdominal viscus. Gonococcal perihepatitis should also be included in this list.

Gonococcal perihepatitis is usually a presumptive diagnosis. Unless these patients are operated upon or have peritoneal lavage, cultures of the perihepatic lesions are not obtained. Percutaneous liver biopsy cannot be generally recommended. Prompt resolution of right upper quadrant pain in association with antibiotic therapy for gonorrhea allows the diagnosis to be established.

Summary

As the incidence of gonorrhea increases, it is probable that more cases of gonorrheal perihepatitis will be seen. Although trauma has been implicated in the etiology of Fitz-Hugh-Curtis Syndrome, substantiation has been difficult. We have presented two cases of this syndrome in which trauma was initially felt to be responsible for right upper quadrant abdominal pain. The diagnosis was based on a positive culture for *Neisseria gonorrhea* and resolution of the pain on adequate therapy. If this diagnosis is considered and confirmed, exploratory laparotomy or extended hospitalization may be obviated and early, appropriate treatment may be instituted. •

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Thyrotoxicosis in the elderly*

Robert E. Cutler, MD, Espanola

TOXIC NODULAR GOITER is a disease of the thryoid which has particular significance in the elderly patient. Nodular goiters are very common with advancing age, and the incidence of thyrotoxicosis, contrary to common belief, increases with age. Toxic nodular goiter is frequently masked in the elderly patient by cardiac, neurologic, or other manifestations which may be attributed to primary disease of the affected organ systems or to the aging process itself. The disease is frequently present for many years before the diagnosis is made, resulting in progressive and often irreversible deterioration of the health of the patient. Finally, the problem of thyrotoxicosis is infinitely more complicated in the older patient.

Causes of Thyrotoxicosis

A classification of thyrotoxicosis is presented in Table 2. Classic Graves' disease with diffuse goiter and exophthalmos was described in the early 1800's by Parry, Graves, and Von Basedow. In 1913, Wilson and Plummer at the Mayo Clinic separated patients with thyrotoxicosis due to multiple functioning nodules from those with classic Graves' disease, and recognized that these patients did not develop some of the features of Graves' disease, such as exophthalmos and dermopathy.[1-3] A solitary toxic adenoma is seen more frequently in young indivduals, but may occur at any age. Except for excessive doses of exogenous thyroid medication, the other causes of thyrotoxicosis listed are rare and not the concern of this presentation.

TABLE 1

OVERALL NEW CASES

	AGE IN YEARS							
	20-29	-39	-49	-59	-69	-79	-89	TOTAL
No. of Males	1			2	4			8
No. of Females	4	6	5	3	13	7	3	41
TOTAL	5	6	5	5	17	8	3	49

← 21 —*— 28 →

(57%)

TABLE 2

CLASSIFICATION OF THYROTOXICOSIS

I. Graves' disease
    Parry (1825) - Graves (1835) - VonBasedow (1840)
    Toxic diffuse goiter with exophthalmos
    Graves' disease with functioning nodules
    (Marine-Lenhart Syndrome)
II. Toxic multinodular goiter
    Plummer's disease
    Toxic nodular goiter
III. Toxic Adenoma (uninodular)
IV. Excess thyroxine or T3
    A. Exogenous-Thyrotoxicosis factitia, medicamentosa
    B. Follicular carcinoma of thyroid
    C. Struma ovarii
V. Excess TSH production
    A. Pituitary tumor
    B. Ectopic TSH production
        Choriocarcinoma
        Hydatid mole
VI. Iodine administration in nodular goiter (Jod Basedow)

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*Presented at the American Geriatric Society Symposium, Santa Fe, New Mexico, June 13, 1975.

TABLE 3
THYROTOXICOSIS AND GOITER

I. Toxic multinodular goiter (Plummer's disease)
  Multiple autonomous functioning nodules
  Suppressed normal tissue present

II. Graves' disease
  A. Classic - Toxic diffuse goiter with exophthalmos
  B. With nonfunctioning nodules
    Simple, nontoxic multinodular goiter
  C. With functioning nodules
    1. Co-existent toxic nodular goiter (Plummer's disease)
    2. Incidental functioning nodules (adenomas)
      Marine-Lenhart Syndrome
  D. Coexistent Hashimoto's disease
    Diffuse or nodular goiter

TABLE 4
DIAGNOSIS OF THYROTOXICOSIS IN THE ELDERLY

I. Clinical manifestations
  A. Symptoms and signs
    1. Sweating, tremor, tachycardia, lab data (same incidence, all ages)
    2. Multinodular goiter, absence of goiter, absence of eye signs, duration of disease, weight loss, atrial fibrillation, CHF, atypical or masked forms (increased incidence over age 60)
  B. Masked hyperthyroidism
    1. Classic, but minimal, symptoms and signs
    2. Cardiac
    3. G.I.
    4. Apathetic

II. Laboratory data and diagnosis
  1. Need to test elderly on minimal and wide indications
  2. Tests usually abnormal, but may be minimally so.
  3. Frequently normal single test

Pathogenesis

The pathogenetic mechanisms of thyrotoxicosis are not always apparent in a toxic patient with a multinodular goiter. Another way of looking at the problem based on our knowledge of pathogenesis is shown in Table 3. The patient, especially the elderly with a multinodular goiter, may have a toxic nodular goiter (Plummer's disease) with multiple autonomously functioning adenomas. There is an unusually high incidence of thyrotoxicosis in patients with pre-existing multinodular goiter. The reasons for loss of normal feedback control and regulation are unknown. The cause of endocrine adenomas in any gland is unknown, but the origin of toxic autonomous goiters is generally envisioned as a small, TSH independent, area (or areas) of hyperplasia and hyperfunction.[4] Hyperthyroidism develops when hyperplasia exceeds degeneration and involution. This requires a nodule at least 3 to 4 cm. in greatest diameter. Spontaneous cure of hyperthyroidism may result from hemorrhage into the nodule, and degeneration and cyst formation. The hyperfunctioning nodules are not suppressed by administration of T3 or T4, nor stimulated by the administration of TSH.[5] They are invariably associated with suppressed normal tissue which can be identified histologically in surgical specimens or be demonstrated by the RAI uptake and scan after the administration of TSH. These patients do not develop the other manifestations of Graves' disease, such as exophthalmos, pre-tibial myxedema, and presence of long acting thyroid stimulator (LATS) in the serum. The solitary toxic nodule, or toxic adenoma, and toxic multinodular goiter are probably the same entity and of identical origin.[4]

The patient may have Graves' disease in a multinodular goiter, instead of the classic picture with diffuse goiter. In contrast to the patients with Plummer's disease above described, the gland in Graves' disease with nodules is characterized by the absence of normal tissue capable of TSH stimulation or T3 suppression. This also can be seen on surgical specimens and demonstrated by RAI uptake and scans.[4] The nodules in patients with Graves' disease may be of variable origin. Graves' disease might develop in a previously existing nontoxic nodular goiter ("colloid goiter"), or coexisting Plummer's disease may be present. In 1911, Marine and Lenhart published their observations on the histopathology and the iodine content of the thyroid gland in exophthalmic goiter and noted the coexistence of fetal and follicular adenomas which concentrated iodine.[6,7] The syndrome of Graves' disease with incidental nodules has been accepted as a subdivision of Graves' disease ever since. In the absence of exophthalmos or other manifestations of Graves' disease, the physical findings in this syndrome may be indistinguishable from Plummer's disease. However, recent studies have shown that the nodules in this form of the disease behave differently from those in Plummer's disease, and the name Marine-Lenhart Syndrome has been proposed for this entity.[8] In this syndrome, the nodules may be stimulated by TSH and their response to RAI therapy, in terms of resistance, and the pattern seen on scans after therapy, differs significantly from that seen in Plummer's disease.

Finally, there is a significant relationship between Graves' disease and Hashimoto's disease (lymphocytic thyroiditis), and a goiter, usually diffuse, but sometimes multinodular, may contain both these diseases in the same gland.[9-12]

TABLE 5
FEATURES OF APATHETIC THYROTOXICOSIS

1. An elderly patient with typical, placid, apathetic facies
2. Small goiter - usually multinodular
3. Presence of depression, lethargy, or apathy
4. Absence of ocular manifestations. Usually have blephartoptosis
5. Muscular weakness and wasting. Proximal myopathy
6. Excessive weight loss
7. Cardiac dysfunction - Atrial fibrillation, CHF

Incidence

While the peak incidence of classic Graves' disease occurs in younger women, the diagnosis of thyrotoxicosis in the older age groups has become more frequent with the recognition of various masked forms of the disease and the availability of more refined diagnostic technics.[13-19] As early as 1939, Cookson, in England, and others began to publish data calling attention to the high incidence of disease in the older patients.[13] In 400 cases seen between 1930 and 1938, 63 per cent were over 40 years of age and 42 per cent over 50 years of age. More recently, Ronnov-Jessen and Kirkegaard in Denmark[19] instituted studies in a county hospital on broad indications, and, over a three-year period, identified 49 patients, 28 (57%) of whom were over 60 years of age. The figures are even more striking if compared to the total number of patients in each population group—during this three-year period, thyrotoxicosis was found in 22 of 7,510 patients over 60 years of age and in 19 of 38,451 patients under 60 years of age, a seven-fold greater incidence in the older age group.

As mentioned earlier, patients with pre-existing nontoxic multinodular goiters are more likely to develop hyperthyroidism than normal individuals without goiters.[20,21] Indeed, a non-toxic multinodular goiter, usually of long-standing, invariably precedes the development of thyrotoxicosis in toxic multinodular goiters. The incidence of hyperthyroidism developing in non-toxic nodular goiters is unknown; one estimate is 13 per cent. Beierwaltes has stressed the frequency by stating that one should always consider thyrotoxicosis to be present in any patient over 40 years with nodular goiter until proven otherwise.[22] The incidence of both Graves' disease and non-toxic multinodular goiters is higher in women than in men, and this is true also for toxic multinodular goiters, as might be expected.

Diagnosis

There are considerable differences in the clinical manifestations of thyrotoxicosis in the elderly patient as contrasted to the younger patient (Table 3). These differences frequently account for the long delay between the onset of thyrotoxicosis and the diagnosis in the elderly patient with multinodular goiter, estimated to average 7 to 7½ years as contrasted to 3½ to 6 months for classic Graves' disease.[22] Features which are common to both age groups include sweating, tremor, tachycardia, and, in general, abnormal thyroid function. Features which are noted to be significantly more frequent in the older group include the absence of exophthalmos and other eye signs, increased frequency of multinodular goiter, or the absence of a goiter, increased weight loss, and the frequent occurrence of monosymptomatic, oligosymptomatic, atypical, or masked forms of the disease.[13-19,23-30]

Masked forms of the disease are characteristic of thyrotoxicosis in the elderly. Four basic types encompass most cases. First, there are those patients in whom most of the features are not atypical, but the symptoms and signs are minimal and often overlooked, or simply attributed to aging or other coexisting disease. In these patients, thyroid function may also be minimally abnormal or borderline, and single tests are frequently normal. Second and third are the monosymptomatic forms of masking in which disturbances of one system are prominent and suggest primary disease of that system, most commonly presenting as cardiac or gastrointestinal disease. Atrial fibrillation, congestive heart failure, and angina pectoris are common in elderly patients with thyrotoxicosis, and the first clue to the physician may be an unusual resistance or lack of response to digitalis. Gastrointestinal masking, with nausea, vomiting, abdominal pain, or diarrhea, was first described by Hamburger and Lev in 1930, and shortly thereafter by others, and is frequently mentioned to the present time.[25-27,29]

Fourth, there is the apathetic form, and as with so many facets of thyroid disease, earlier writers have already defined and described it with a completeness and eloquence which cannot be improved upon today. Hamburger and Lev (1930) credit Lahey for the first description and definition of this entity:[25]

> "These patients are for the most part at or near the middle decade of life—individuals without exophthalmos, struma or tachycardia. The majority of them, ward patients, poor, burdened with countless worries, apathetic, listless, with masked facies, dulled eyes, quiet and insensitive, are in striking contrast to the alert, restless, nervous, bright, prominent-eyed patient with hyperthyroidism".

And Lahey's own writing (1930) is equally eloquent and even more complete:[23,24]

> "All that is so positive in activated hyperthyroidism, however, is negative in apathetic or non-activated hyperthyroidism . . . Apathetic thyroidism appears almost entirely in those patients of middle age and past middle age . . . patients with apathetic thyroidism tend to have no exophthalmos and little, if any, stare . . . to have small, firm glands without striking increase in size . . . to have relatively low pulse rates varying from 100 to 120, and not characteristically full and bounding in character . . . the apex beats are not striking, distinctly not forceful, and obviously unimpressive in character . . . there is very definite repose, reaching in many instances to a definite apathy which leads us to designate it by this term . . . patients with apathetic thyroidism have their appearance of ageness exaggerated until they seem unduly old for their actual years . . . the skin tends to be dry, cool, lifeless, and with the pigmentation which characterizes old age . . . they die in states of distinct apathy progressing into coma . . . patients with serious and fatal reactions following partial thyroidectomy for apathetic thyroidism go back to their beds and either never awaken from their anesthetic, or awaken only to sink comfortably, leisurely, without activation, into semi-stupor or to become completely unconscious and die gently with practically none of those awesome activation signs which accompany death with the typical activation thyroidism as, for example, seen in a young girl with intense exophthalmic goiter".

Apathetic thyrotoxicosis is frequently associated with the other types of masking, especially cardiac. This form of disease is most commonly seen in older patients, but apathetic thyroid storm has been reported in a ten-year-old child.[31] Thomas et al, have most recently reviewed this entity in 1970, and stress the typical appearance of these patients with a characteristic facies.[30] Clinical characteristics listed by Thomas are shown in Table 4. Thyroid function tests in these patients are almost always abnormal and the diagnosis is usually easy once it is considered. However, elevations of T4, RAI uptake and T3 resin uptake may be minimal. It should be emphasized that the T3 suppression test may be dangerous to these patients.

A few comments should be made concerning the laboratory data and diagnosis of thyrotoxicosis in the elderly. Because of masking and coincidental diseases, one must consider the diagnosis and test the elderly on minimal and wide indications. Thyroid function tests are usually abnormal, but may be minimally so. A single test is frequently normal, so that several tests should be run when the disease is suspected. A T4 level, 24-hour RAI uptake, and a T3 resin uptake will usually provide the diagnosis. Again, the T3 suppression test in which Triiodothyronine (Cytomel) is usually given for a period of 4 to 7 days or longer to test suppression of the RAI uptake may be dangerous to these patients, especially in those with cardiac manifestations or apathy.

Treatment

In a brief consideration of treatment of the elderly thyrotoxic patient, several points need to be emphasized. Patients with multinodular toxic goiters are relatively resistant to any form of therapy, whether it be irradiation with RAI, anti-thyroid medication, or surgery. Because of the cardiac manifestations in this age group, treatment should be instituted as soon as the diagnosis is made. Once cardiac complications such as congestive heart failure develop, they are often irreversible and are usually difficult to treat, even though the thyrotoxicosis is subsequently corrected. If cardiac manifestations are prominent, the disease should be brought under control medically with Tapazol or Propylthiouracil before giving RAI. These drugs may then be discontinued 48 hours before RAI is administered and resumed 48 to 72 hours after RAI with little or no loss in efficacy. The dose of RAI needs to be larger in multinodular goiters, with or without Graves' disease (in the range of 10-25 mc.) and repeat doses are more frequently required than in diffuse goiters and younger patients. TSH should not be given before the administration of RAI in an attempt to increase the uptake of the nodules; the autonomously functioning nodules in toxic multinodular goiter (Plummer's disease) do not respond to TSH and one only stimulates the uptake of radioactive material by the suppressed normal tissue.[32] This normal tissue will prevent the patient from developing hypothyroidism secondary to RAI therapy because it is suppressed by the hyperfunctioning adenomas and does not take up RAI. Once the adenomas are destroyed by RAI, suppression is terminated, and the normal tissue recovers normal function. Patients with large goiters, or with compression symptoms, or those in whom possible malignancy is suspected, are best treated surgically. •

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* Because of limitation of space this list of 32 references has been abbreviated by omitting those references which were entered primarily to identify reports of a case or technic of a laboratory examination. The complete reference list may be obtained from author.

Laminaria in abortion*

Use in 1368 patients in first trimester

Warren M. Hern, MD, MPH, Boulder, Colo.

DURING RECENT YEARS, there has been a revival of interest in the use of laminaria in the United States.[1-6] There appear to be various advantages in the use of this material for cervical dilatation, especially in first-trimester abortion. Laminaria is a species of seaweed, hydroscopic when dry, and dilates three to five times its diameter when wet. The physiologic principle of relatively atraumatic dilatation has great appeal, and the use of gas sterilization seems to have overcome earlier problems with excessive infection rates.[7,8]

In November, 1973, a private, non-profit community abortion clinic† was opened in Boulder, Colorado, to help with the unmet need for inexpensive first-trimester abortions in that state and community. One of the principal foundations of the original medical policies was the use of overnight cervical dilatation with laminaria because of the advantages in medical safety offered by this method. A strong counseling program was instituted simultaneously, with both medical and counseling programs building on precedents established earlier by Planned Parenthood, Preterm, and other such first-class abortion facilities in New York and Washington, D.C.

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*This paper was presented at the American Public Health Association Meeting, New Orleans, October 21, 1974. Dr. Hern is the director of the Boulder Abortion Clinic, Boulder, Colorado, and former Medical Director of the Boulder Valley Clinic.

†Boulder Valley Clinic

Materials and Methods

Primary contact with the clinic for most patients was through a telephone request for appointment. Patients with a last menstrual period date of more than 11 weeks in length or gestation of more than 9 weeks were usually referred elsewhere. Occasional patients with 10 weeks gestation were accepted due to hardship circumstances. Patients with histories of hypertension, bleeding tendencies, neurologic disorders, extreme obesity, hospitalization for mental illness during the previous year, asthma requiring recent hospitalization, diabetes, significant heart disease, acute or chronic pelvic infection, more than five full-term pregnancies, or a desire for general anesthesia were referred elsewhere or to the Medical Director for consideration.

Upon initial acceptance, the patient was required to provide proof of a recent pelvic examination with an estimate of gestational age, or have a screening examination by the clinic physician or nurse. Following this step, the patient had her laboratory work performed at the clinic and filled out a personal information and medical history form. She was then assigned to an individual counselor who spent forty-five minutes to one hour reviewing the circumstances of the pregnancy with the patient, her knowledge of reproduction, contraceptive methods, and the nature of the abortion procedure. This was followed by a brief interview with the clinic physician, physical examination, and placement of the laminaria.

At the time of the pelvic examination a gonorrhea culture was taken in all patients unless they had had one during the previous week, and a Papanicolau smear was taken if indicated. The vagina was prepped with a dilute povidine-iodine solution, and the cervical canal sounded to just past the internal os to determine patency and direction. If necessary, a single-tooth Schroeder tenaculum was placed laterally to stabilize the cervix and to straighten the endocervical canal. The laminaria was then coated with nitrofurazone ointment and placed in the endocervix with Milex laminaria forceps. The vagina was packed with three to four 3 x 3 gauze sponges, the first one being covered with approximately 2cc of nitrofurazone ointment. The patient was advised to call the clinic if she had severe cramps and was advised that she might have a yellowish discharge.

The following morning, the patient returned to the clinic approximately fifteen minutes before her scheduled procedure and was given 5-10 milligrams of Diazepam orally if indicated. Following a recording of her vital signs, the gauze and laminaria were removed under direct vision with sterile ring forceps and a repeat bimanual examination performed to re-ascertain uterine size and position. The vagina was prepped again with povidine-iodine solution and a wheal of approximately 5cc of 1% Lidocaine solution placed on the anterior or posterior cervical lip, depending on the direction of the uterine curve.

At this point, a side-curved Kelly cervical tenaculum (Allis tip) was placed at the site of the anesthesia wheal. A curved, rigid plastic uterine aspiration cannula of an appropriate size was then placed into the uterine cavity. If the uterine fundus was sounded with an early pregnancy, the cannula tip was then withdrawn 1-2 cm to reduce the risk of vacuum perforation of the uterine wall. The suction tubing was then connected. Upon reaching the maximum vacuum, the cannula tip was rotated to facilitate aspiration but not, as a rule, pushed in and out without completely withdrawing the cannula. If withdrawal was necessary to clear the cannula, the suction tubing was disconnected and re-connected with the cannula back in place within the uterine cavity. This permitted use of the blunt cannula as a sound. A slight in-and-out motion was applied, however, when a large placenta could be cleared by gentle tugging with the connected cannula.

Following emptying of the uterus by aspiration, the uterine cavity was explored with a ¼-curve Randall kidney stone forceps or a ⅛-curve fenestrated uterine dressing forceps depending on the amount of dilatation. This was followed by sharp curettage and re-aspiration if necessary. Oxytocics were administered parenterally as necessary.

The patient was then observed in an adjacent recovery room for at least one hour, given her postoperative instructions and a followup appointment for three weeks later. Antibiotics or other medications were not given postoperatively unless specifically indicated.

Results

During the first fourteen months of clinic operation, 1406 abortion procedures were performed. Twelve of these were performed on previous patients. All but 38 (2.8%) were performed following cervical dilatation with laminaria. Reasons for manual dilatation included heavy bleeding following initial endocervical sounding (two cases), presumably due to the presence of a placenta praevia, scheduling problems, or difficulty placing a laminaria.

The median age of the patients was 21 years, with 4.1% being under 17, 57.8% being between 17 and 22 years of age, and 0.4% being 40 years of age or over. Twenty-nine per cent of the patients were from the Boulder area, 28.4% from the Denver metropolitan area, 36.7% from the rest of Colorado, and 5.9% from neighboring states. Thirty-nine per cent of the patients had had previous pregnancies, and 18.1% had had previous abortions. 1.8% of the patients had already experienced two abortions, and .2% had had three or more. For 68 patients (4.8%), the current abortion was the second within one year.

About 40% of the patients were referred by public or private agencies such as Planned Parenthood and health departments, 20.3% by private physicians, and the remainder by friends, former patients, or themselves as the result of initial publicity surrounding the clinic's opening. The overall followup rate, including letter and phone contact, was 80%, with 55% of patients seen in the clinic for a followup examination. Consistency of methods was enhanced by the fact that one physician (WMH) performed all but 3% of the procedures and provided nearly all followup care.

A final estimate of length of gestation indicated that over 65% of the pregnancies terminated were between 5 and 8 weeks duration, with about 10% being under 5 weeks, 18.1% from 9 to 10 weeks, and 4.6% 11 weeks or more. 1.1% of the procedures resulted in no evidence of pregnancy.

Of the 1368 procedures accomplished with the use of laminaria, 133 or 9.4% were accompanied by secondary manual dilatation with Pratt dilators. As an indication of the value of experience in reducing this proportion, it may be noted that 20 of these cases occurred in the first 102 procedures, and a substitute physician in ob-gyn residency training who performed 42 of the procedures had a manual dilatation rate of 28.5%. The remaining 1224 cases had a secondary dilatation rate of 8.3%.

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The most common cause for manual dilatation was inadequate dilatation by the laminaria. In the early patients, however, it was primarily the result of uterine expulsion of the laminaria. This problem was remedied by adequate gauze packing. In some of the more advanced pregnancies, manual dilatation merely supplemented the basically adequate dilatation provided by the laminaria. This was felt to be desirable to allow greater ease and speed in completing the procedure.

Some maneuvers proved to be especially helpful in adequate placement of the laminaria. One was adequate sounding through the internal os, sometimes leaving the sound in place for a minute or two, then being sure that the terminal tip of the laminaria was through the internal os. Having an assistant put pressure on the uterine fundus by pressing downward behind the symphysis seemed to help straighten the endocervical canal in combination with cervical traction enough to allow passage of a very straight laminaria.

Another special problem was presented by the very early (4-5 week) pregnancy, particularly in the primagravida. Here, it frequently seemed desirable to have the patient return to the clinic early in the morning, dilate the cervix very slightly with the smallest Pratt dilator (#13 French), just enough to admit a "thin" laminaria. The patient was then instructed to return four hours later for her procedure. Supplemental manual dilatation was frequently necessary under these circumstances, but it was facilitated by the softening provided by the laminaria.

One very notable problem presented by the use of laminaria is the "dumbelling" or the development of differential expansion. This phenomenon can be very disconcerting, especially to the operator who is unfamiliar with its diagnosis and management. Sometimes the laminaria will expand more in the distal portion past the internal os than at the level of the internal os itself. When this happens, the operator is unable to remove the laminaria. It is frequently associated with severe cramping during the night or during an attempt to remove it. If the patient calls and is instructed to remove it herself or have it removed by her husband or companion, she will probably be spared a more prolonged process of removal the next morning. The author has received reports of attempts to push the laminaria into the uterus upon discovery of this condition with resulting complications including perforation and hysterectomy. There has been at least one published report of a similar problem.[9] A maneuver which appears to be completely safe and effective in the management of this situation, however, is the application of a thorough paracervical block accompanied by gentle, steady traction with ring forceps. With a very difficult extraction, this can be assisted by grasping the laminaria at a point just below the internal os with a pair of curved uterine packing forceps. This was necessary in only one difficult case, but it proved to be invaluable. The "dumbelling" phenomenon (or "hourglass effect", since it results in an hourglass-shaped laminaria) occurred 1.8% of the time in this series. One-fourth of these 25 cases required additional manual dilatation. Since 64% of the cases of "dumbelling" occurred in pregnancies of 6 weeks' gestation or less, it would appear that many very early cases might be best managed by a 4-5 hour laminaria placement rather than the overnight placement.

TABLE 1

COMPLICATIONS WITH LAMINARIA

IMMEDIATE		
Hemorrhage, post-laminaria		1
Atony, operative, with hemorrhage (up to 250cc blood loss)		6
Atony, postoperative (within 4 hours)		2
Laminaria removed due to pain		5
Anesthesia reaction		1
Septicemia, gram negative (one hour post-op)		1
Retained tissue		1
Convulsion		1
False passage of laminaria		1
		19
DELAYED (within 4 weeks after procedure)		
Fever (102° or less, less than 1 day)		58
Endometritis/parametritis		11
Treated with antibiotics (above two categories)	(18)	
Severe cramps		14
Superficial thrombophlebitis		1
Retained tissue		1
Depressive reaction		4
Combined (bleeding, cramping)		6
Cystitis		1
		96
LATE (more than 4 weeks after procedure)		
Pelvic abscess		1
TOTAL COMPLICATIONS	= 116/1406	= 8.3%

One critical aspect to the "dumbelling" phenomenon is the sturdiness of the laminaria material itself. It is obvious that a laminaria that disintegrates under the kind of traction necessary to remove one which has "dumbelled" is unsatisfactory and dangerous. Of the 1368 procedures performed with laminaria, all but three were accomplished with Milex® brand *(laminaria japonicum),* single-time use. Nineteen of the 21 cases of dumbelling occurred with Milex® laminaria, and in one of these, the string at the proximal end pulled through, but the laminaria was removed under paracervical block with relative ease. A quantity of Eschmann® laminaria *(laminaria digitata)* were obtained for use upon recommendation by a colleague, but were generally found to be too large for first-trimester pregnancy. Three were placed in one afternoon session. Two "dumbelled" and both disintegrated the following morning with traction, requiring a long and tedious process of removal with no adverse consequences.

Blood loss was generally minimal. Eighty-five per cent of the procedures resulted in approximately 20-30 cc blood loss, and 95% of the procedures caused 50cc or less blood loss. In seventeen procedures there was over 100cc blood lost (1.6%), with six procedures (0.4%) being accompanied by as much as 250cc blood loss. These results may be compared to those obtained by Niswander.[10]

The overall complication rate, 8.2%, is similar to the 8.0% rate described in 1972 by

Newton, but contains more categories.[11] The complications are listed in Table 1. They include the minor complaints of postabortion bleeding and cramping which were more than a normal menstrual period. They also include five cases of excessive bleeding during the procedure, one case of overnight post-laminaria bleeding requiring immediate attention and completion of procedure, and four cases in which severe cramping required home self-removal of the laminaria. It includes one case of tubo-ovarian abscess requiring laparotomy which occurred some seven weeks after the abortion and nearly four weeks after a completely normal followup examination. There is no conclusive evidence to date which clearly relates this latter development to the abortion or, for that matter, suggests any other cause. The complications also include two cases of postabortal uterine atony (0.2%), which may be compared to the 0.88% reported by Sands and Burnhill.[12] There were no uterine perforations, cervical lacerations, or continued pregnancies.

The most significant set of complications were those related to infection or fever. One patient developed chills and fever of 102° approximately one hour after her abortion as she was preparing to leave the clinic. Blood cultures were taken, and these and endocervical and uterine cultures grew out E. Coli. Re-aspiration revealed a few small clots. Prompt antibiotic therapy resulted in a remission of symptoms and there were no further complications. Of all patients, 5.5% developed fevers, almost all less than 102° and of a transitory nature. Eighteen patients either presented themselves for treatment during or within 12 hours after the febrile episode and were treated with Doxycycline 100 mgm b.i.d. (1.2%). Eleven patients (0.8%) were diagnosed as having endometritis or parametritis.

There were five patients who were known to have been hospitalized. One was hospitalized with heat stroke following a raft trip taken a few days after the abortion, contrary to postoperative instructions. Another was hospitalized because of anxiety in both the patient and the clinic physician during the second week of clinic operation after the patient reported an episode of heavy bleeding and passage of clots; her overnight hospital stay and subsequent course was entirely uneventful. A third reported bleeding and cramping approximately one week after her procedure, was seen at a hospital in her locality where she was re-aspirated and found to have a small quantity of intrauterine clots. A fourth was treated for endometritis by a colleague in a neighboring state on the third postoperative day, and the fifth was the patient who developed a tubo-ovarian abscess some seven weeks after her abortion.

Discussion

During the first fourteen months of clinic operation, the use of laminaria proved to be a highly acceptable component of treatment in the termination of first-trimester pregnancy. One day in which all patients had manual dilatation, because of scheduling difficulties, was enough to convince the entire clinic staff, all of whom had had ample previous experience in clinics where manual dilatation was standard, of the value of the laminaria technic. Basically, it seems not only much easier on the patients but also on the operating physician.

The principal disadvantages include the necessity for two clinic visits, the risk of mild to severe overnight cramping (seen to some extent in perhaps 1/3 of all patients), expense (Milex laminaria cost $2.75 each), and occasional anxiety about whether the patient is responsible enough to return the following day. This latter possibility was never a serious problem, however. Initially, we were concerned that patients would experience an increase in anxiety during the overnight wait. However, in the vast majority of patients, the opposite tended to be true.

The medical advantages have appeared to be significant. Most importantly, the use of laminaria offers a safe, physiologic, atraumatic method of cervical dilatation. There is a reduced need for local anesthesia and a decreased likelihood of a serious anesthetic reaction. There is a reduced risk of uterine perforation and cervical laceration due to the lessened need for forceful dilatation. The procedure time is rapid, and blood loss is usually insignificant if not nonexistent. Finally, it allows some careful preoperative evaluation of the patient's emotional status, her reaction to the pregnancy and abortion, and her response to pain prior to the actual procedure. The complication rate seems comparable to or better than those seen in other series.[13-15]

Summary

The use of laminaria for cervical dilatation has gained recent acceptance in the United States for use in first-trimester abortions. Since 1973 in a community abortion clinic in Boulder, Colorado, laminaria has been used almost exclusively for cervical dilatation. During the first 14 months of clinic operation, over 1400 first-trimester abortion procedures were performed. Laminaria was used in 1368 of these. There were no uterine perforations or cervical lacerations, primarily because the technic markedly reduced the need for forceful manual dilatation. The chance of anesthetic reaction is lessened because of the reduced need for local anesthetic. There has been only one major complication.

The use of laminaria appears to have significant advantages for patient safety in first-trimester abortion. •

ACKNOWLEDGEMENTS

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DRUGS MENTIONED IN TEXT

Diazepam (Valium)
Povidine-iodine solution (Betadine)
Nitrofurazone (Furacin) soluble dressing
Lidocaine (Xylocaine)
Laminaria japonicum (Milex)
Laminaria digitata (Eschmann)
Doxycycline hyclate (Vibramycin)

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Less than a cancer operation for breast cancer?

Gifford V. Eckhout, MD, Denver

An extraordinary amount of lay and medical publicity in recent years has created an impression that simple mastectomy, or even lumpectomy, is as effective as radical mastectomy in treating breast cancer. It is time, and important, that physicians review the facts.

The Halsted radical mastectomy became popular because lumpectomy or simple mastectomy produced miserable results with practically zero ten-year survivals and 65 per cent local recurrence. The Halsted operation has remained the standard form of treatment of breast cancer. However, beginning in 1941, McWhirter began to challenge the standard method and introduced simple mastectomy plus irradiation as an alternative treatment. Kaae and Johansen[1] have reported their results with this modality and have classified their patients using the Columbia Clinical Classification allowing comparison with other studies using the same classification. The ten-year survival figures are 50 per cent and 32 per cent respectively in Stage A and Stage B for simple mastectomy and irradiation compared to 63 per cent and 37.5 per cent as reported by R. S. Handley for the modified radical mastectomy and compared to 70 per cent and 43 per cent as reported by C. D. Haagensen for the Halsted radical mastectomy (Table 1). Recently, Haagensen[2] reclassified his cases according to the International TNM classification so that his results could be compared with those of McWhirter. This comparison shows a ten-year survival of 54 per cent and 43 per cent respectively for Stage I and Stage II reported by McWhirter using simple mastectomy and irradiation with a survival of 78 per cent and 55 per cent in Haagensen's series using the Halsted radical mastectomy (Table 2).

It is not surprising that ten-year results with lumpectomy or simple mastectomy are inferior to those obtained by radical mastectomy when one considers that in nearly 60 per cent of operable cases of breast cancer axillary nodes contain cancer and are left behind with simple mastectomy.[3] Also lumpectomy fails for the same reason plus the fact that some 50 per cent of operable breast cancer cases have nonpalpable foci of cancer elsewhere in the same breast that are not removed with lumpectomy.[3]

TABLE 1

Carcinoma of the Breast
Columbia Clinical Classification
Comparison of ten-year survival

Columbia Classification	Kaae and Johansen 187 Patients Simple Mastectomy and Irradiation	Handley 160 Patients Modified Radical	Haagensen 609 Patients Radical Mastectomy
Stage A	50%	63%	70%
Stage B	32%	37.5%	43%

TABLE 2

Carcinoma of the Breast
International TNM Classification
Comparison of 10-year survival rates
in patients under 65 years of age

	McWhirter Simple Mastectomy and Irradiation		Haagensen Radical Mastectomy	
	Patients	10-year Survival	Patients	10-year Survival
Stage I TNM	600	54%	360	78%
Stage I TNM	491	43%	137	55%

TABLE 3

Carcinoma of the Breast
Ten-year Survival
Crile and others[1]

	Stage	Treatment	Number	10-year Survival
Crile	I & II	Simple	69	48%
Crile	I & II	Modified Radical	62	34%
Payne	All operable	Radical	2171	59.4%
Anglem and Leber	Columbia A & B	Radical	94	60%
Finney	All operable	Radical	71	55%
*Haagensen	A & B	Radical	794	63.5%
*Handley	A & B	Modified Radical	251	53.7%

*Added by the author for comparison.

When these lesser operations are performed, often dependence is placed on irradiation to destroy the remaining cancer. However, irradiation alone or in combination does not give results equal to radical mastectomy. Baclesse[4] reports 40 per cent ten-year survival using irradiation only for Columbia Classification Stages A and B breast cancers; Peters[3] reports 44 per cent ten-year survival using local excision and irradiation for International TNM Stage I breast cancers; Miller[5] reports 40 per cent ten-year survival using simple mastectomy only for Columbia Classification Stage A breast cancer, while Haagensen reports 74.5 per cent ten-year survival with radical mastectomy for Stage I breast cancer.

Crile has been the most outspoken critic of the radical mastectomy and has devoted much time trying to convince doctors and patients alike that radical mastectomy should be abandoned. A critical review of the facts indicate that radical mastectomy remains the superior form of treatment for breast cancer. Crile's results are compared in Table 3, and in each instance his results are inferior to radical mastectomy. These differences in ten-year survival become even more significant when one studies Crile's report in *Annals of Surgery* in 1968,[6] in which there is obvious bias in case selection. To illustrate the extent of bias in Crile's work, here reproduced in Table 4, is Crile's Table 2 from the above publication. As pointed out by Anglem and Leber,[7] Crile's footnote to this Table 2 is more significant than the figures of the chart. The footnote states that of 27 breast cancers under 1.5 cm. in diameter, 26 were treated by simple mastectomy, so almost all of the most favorable tumors were allocated by selection to the group treated by the simple operation, and the survival statistics of the table for radical mastectomy are for the patients with tumors over 2.7 cm. in diameter. Also it should be noted that many reports exist in the literature with better five-year survival rates using radical mastectomy than reported by Crile for these 27 selected cases. For example, Payne[8] reports 1205 radical mastectomy patients with negative nodes with 86.4 per cent five-year survival.

Some critics of radical mastectomy, Crile being the most outspoken, theorize that the axillary nodes offer immunity to the patient with breast cancer and that therefore these nodes

TABLE 4

Carcinoma of the Breast
(Crile's Table 2)[6]

Five year survival rates of comparable "True Stage I" patients treated by simple mastectomy or by radical mastectomy with or without irradiation* 1955 through 1962.

Treatment	Number Patients	Average Size Cm.	Average Age Years	Survivors Number	Percentage Surviving 5 Years
Radical, with or without Cobalt	43	2.7	56	28	65
Simple, without Cobalt	94	2.8	58	77	82
Simple, with Cobalt**	16	3.0	59	11	69

*All patients had invasive operative Stage I Cancers. Patients with cancers less than 1.5 cm. in diameter were excluded because patients with small tumors were often selected for simple operations. The survival rate of the patients with cancers less than 1.5 cm. in diameter treated by simple mastectomy was 22/26 (85%). The one patient with a tumor less than 1.5 cm. in diameter treated by radical mastectomy survived 5 years.

** Because these were irradiated, the status of the axillary nodes is not known.

TABLE 5
(Haagensen[3])

Carcinoma of the Breast
Columbia Clinical Classification
Local recurrence within 10 years

Clinical Stage	Author	Method Treatment	Number Patients Treated	Local Recurrence Within 10 years
Stage A	Miller	Simple mastectomy only	115	37%
	Kaae and Johansen	Simple mastectomy and irradiation (McWhirter)	159	19%
	Handley	Modified radical mastectomy	160	16%
	Haagensen	Radical mastectomy	609	6.5%
Stage B	Miller	Simple mastectomy only	34	50%
	Kaae and Johansen	Simple mastectomy and irradiation (McWhirter)	28	32%
	Handley	Modified radical mastectomy	91	26%
	Haagensen	Radical mastectomy	185	18%

should not be removed. Clinical evidence does not support this theory. Crile reported simple mastectomy on 110 patients with Stage I disease with a five-year survival of 80 per cent as compared to Payne's report above with a five-year survival of 86.4 per cent. If axillary nodes increased the host resistance, the survival rate should have been better in Crile's 110 patients in whom the axillary nodes remained in the patient. Anglem and Leber state "that there is not a single shred of evidence to say that axillary nodes offer any immunity whether involved or not."

Students of breast cancer have noted many times that the superiority of radical mastectomy over lesser operations becomes even more apparent after the 10-year survival period.[9,10] As an example, Anglem and Leber[7] report fifteen-year survival percentages of 50 per cent for the radical mastectomy compared with 36.8 per cent for simple mastectomy for Stage I breast cancer.

It should also be noted that old age in itself is not a contraindication of radical mastectomy. For example, the Metropolitan Life Insurance tables show that a woman aged 74 has 10.3 years life expectancy remaining. Accordingly, an older woman should not be denied the chance of longer survival afforded her by a radical mastectomy simply because of her advanced age.

Local recurrence is an important consideration in any form of therapy for breast cancer. Comparative studies reveal that radical mastectomy is also superior in this regard. At ten years Haagensen had 6.5 per cent local recurrence with radical mastectomy compared to 37 per cent in Miller's series with simple mastectomy for Stage A breast cancer in each series, and comparison of local recurrence for Stage B is similar (Table 5). These results are in direct opposition to Crile's statement that a Halsted radical mastectomy is designed to create local recurrence because of damage to the skin flaps.

Some critics have stated that Haagensen's results are not comparable to results of others because of case selection. However, when Haagensen includes his more advanced breast cancer cases as determined by biopsy prior to decision for operation, his series show a definite advantage of radical mastectomy over other lesser surgical procedures.

In this paper there has been no attempt to compare the results of modified radical mastectomy with preservation of the pectoralis muscles to the Halsted radical mastectomy with removal of pectoralis muscles. In most large studies a slight superiority is noted for the Halsted radical mastectomy over modified radical mastectomy. More detailed studies with ten-year followup results are necessary to settle this problem. In this regard, however, one should note that in Payne's[8] study of 2571 radical mastectomy operations, the Halsted radical mastectomy gave significantly better ten-year survival rates if the axillary nodes were involved, than those obtained with the modified radical mastectomy when axillary nodes were involved. The ten-year survival rates were 35.8 per cent with the Halsted radical mastectomy compared to 13 per cent with the modified radical mastectomy.

Conclusions

1. When subjected to close scrutiny the studies advocating lesser operations in the treatment of breast cancer are found to be grossly biased in selection of patients for the lesser operation. Despite this bias, radical mastectomy results are far superior in most hands.

2. There is no evidence in the surgical literature of treatment of breast cancer to indicate that any treatment modality is as effective as surgical removal of involved axillary lymph nodes. This becomes particularly important when one considers that in Columbia Classification Stage A, in which there are no palpable axillary nodes, 40 to 50 per cent of patients have axillary metastasis.

TABLE 6
(Haagensen[2])
Carcinoma of the Breast
Columbia Clinical Classification

Clinical Stage	Miller 1927-56				Haagensen 1935-July 1963 Irradiation only			
	Simple Mastectomy only		Radical Mastectomy		Biopsy Proven Metastases Internal Mammary or Subclavicular Nodes		Combined Series of Patients	
	No. Patients	10-year Survival	No. Patients	10-year Survival	No. Patients	10-year Survival	No. Patients	10-year Survival
Stage A	115	40%	609	70%	33	21%	642	67%
Stage B	34	26%	185	43%	53	19%	238	38%

3. When discussing the choice of treatment the physician has a moral obligation to inform his patient with breast cancer of the superiority in survival rates with radical mastectomy over lesser operations for operable breast cancer.

4. The radical mastectomy remains today the best treatment for operable breast cancer.●

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Plans Being Finalized for First Annual Rural Health Conference in October

Improved health care delivery is still a great concern in many rural communities. Isolation presents a special set of problems. Fragmentation of effort in dealing with health care delivery seems an eternal frustration.

We have seen increasing demands on the Colorado Medical Society during the past several years to make political and policy decisions which have been very time-consuming. Consequently, some practical and technical jobs have been left undone.

It seems to me that many rural health care problems do have solutions. It also seems that collectively we have not made efforts to solve some of these problems. During this past year the Colorado Medical Society has become more active in attacking rural health care delivery problems. A multidisciplined approach has been favored.

Accordingly, the first annual statewide **Rural Health Conference** has been planned by CMS for **October 23, 24, and 25** at **Colorado State University** in **Fort Collins.** The Colorado Medical Society, the Colorado Hospital Association, and the Colorado-Wyoming Regional Medical Program will co-sponsor the Conference.

All disciplines of health care delivery will be involved. Invitations are being sent to MD's and DO's, various medical specialists, dentists, and those assisting them in their offices; hospital administrators and their board members, county commissioners, state legislators, nurses, technicians, recruitment committee members, representatives of communities without doctors, representatives from teaching institutions, and many, many more.

The Conference will be based on a problem-solving interdisciplinary format. Keynote speaker will be Dr. Hughes Andrus, Chairman of the Department of Family Practice at the University of California at Davis. Dr. Grady Stumbo of Hindman, Kentucky will demonstrate the interdisciplinary team approach to ambulatory health care delivery on a county basis. Colorado Governor Richard Lamm has also been invited to address the Conference. Caucuses between groups which can solve immediate problems are being arranged.

If you are interested in attending, and have not received an invitation to this first annual Rural Health Conference by September 12, please contact Virginia Bell at the Colorado Medical Society Executive Office, 1601 East Nineteenth Avenue, phone 534-8580.

S. Jack Locke, M.D., Chairman
CMS Rural Health Committee

A medical potpourri

Compiled by Andrew M. Babey, MD, Las Cruces, New Mexico

1. "When your next-door neighbours, friends, or patients return from a Carribbean cruise with an enviable tan, admire it, but beware of their well-intentioned gifts of local handicrafts—particularly bongo drums from Haiti. These wooden drums have goat-hide drumheads with a fringe of hair intact. Anthrax is endemic in Haiti and Bacillus anthracis has been isolated from these drums and also from rugs imported from Haiti." Bongo-Drum Disease, *Lancet*, June 8, 1974, p. 1152.

2. "We have demonstrated that effectively treated patients with benign essential hypertension have a normal urinary albumin-excretion rate. Decrease in albuminuria, regression of fundoscopic changes, disappearance of fluorescein-positive spots in retina, and reduction in the transcapillary escape-rate of albumin, during treatment of severe and moderate essential hypertension, further demonstrate the reversible character of the processes involved. If, as suggested by other workers, extravasation of plasma-proteins with subsequent deposition into the vascular wall is involved in the development of angiopathy as a complication to hypertension, our results support the case for an early and effective treatment of hypertension." Increased Urinary Albumin-Excretion Rate In Benign Essential Hypertension, *Lancet*, June 15, 1974, p. 1192.

3. "MARY, MY PATIENT"

Her zigzag fingers barely grip the stick,
and old and bent
and frail and thin
she hobble-stumbles in the room.
Her painful eyes smile sadly dim upon
a blurred world flashing by.
She calls to Death,
but he is too busy,
gloating over uniformed youth.

So who will love you now, Mary,
with your crepe-de-chine neck
and your atrophic womb?
What tender hand will caress your
wrinkled skin,
for are you not a woman still?

So who will love you now, Mary?
I will—
For ten minutes,
Once a month.

Jeffs, S.G., *Lancet*, July 20, 1974, p. 146.

4. "The teaching profession is the only profession that has no definition for malpractice." Cuninggim, Merimon, *Forbes Magazine*, Thoughts on the Business of Life, September 15, 1974, p. 138.

5. "Technology is now forcing upon us a standard of behavior that formerly was expected only of saints." Toynbee, Arnold, *Forbes Magazine*, Thoughts on the Business of Life, September 15, 1974, p. 138.

6. "To sum up: it is wrong always, everywhere, and for anyone, to believe anything upon insufficient evidence." Clifford, W. K., *The Ethics of Belief*, Gateway to the Great Books, Philosophical Essays, 1963, by Encyclopaedia Britannica, Inc., p. 21.

7. "In my own work at universities I have been much struck by the paralysis of thought induced in pupils by the aimless accumulation of precise knowledge, inert and unutilised. It should be the chief aim of a university professor to exhibit himself in his own true character—that is, as an ignorant man thinking, actively utilising this small share of knowledge. In a sense, knowledge shrinks as wisdom grows: for details are swallowed up in principles." Whitehead, Alfred North, *The Aims of Education*, Mentor Books, July, 1949, p. 48.

8. “The conclusion to be drawn from this discussion is, that alike for masters and for men a technical or technological education, which is to have any chance of satisfying the practical needs of the nation, must be conceived in a liberal spirit as a real intellectual enlightenment in regard to principles applied and services rendered. In such an education geometry and poetry are as essential as turning laths.” *Ibid*, p. 55.

9. “The necessity for constant writing and vocal exposition is some slight stimulus to the thought-power of the professional classes. Great readers, who exclude other activities, are not distinguished by subtlety of brain. They tend to be timid conventional thinkers. No doubt this is partly due to their excessive knowledge outrunning their powers of thought; but it is partly due to the lack of brain-stimulus from the productive activites of hand or voice.” *Ibid*, p. 60-61.

10. “Mere literary knowledge is of slight importance. The only thing that matters is, how it is known. The facts related are nothing. Literature only exists to express and develop that imaginative world which is our life, the kingdom which is within us. It follows that the literary side of a technical education should consist in an effort to make the pupils enjoy literature. It does not matter what they know, but the enjoyment is vital. The great English Universities, under whose direct authority school-children are examined in plays of Shakespeare, to the certain destruction of their enjoyment, should be prosecuted for soul murder.” *Ibid*, p. 66-67.

11. “Intellect is therefore a vital force in history, but it can also be a dissolvent and destructive power. Out of every hundred new ideas ninety-nine or more will probably be inferior to the traditional responses which they propose to replace. No one man, however brilliant or well-informed, can come in one lifetime to such fullness of understanding as to safely judge and dismiss the customs or institutions of his society, for these are the wisdom of generations after centuries of experiment in the laboratory of history.” Will and Ariel Durant, *The Lessons of History*, Simon and Schuster, New York, 1968, p. 35.

12. “We conclude that the concentration of wealth is natural and inevitable, and is periodically alleviated by violent or peaceable partial redistribution. In this view all economic history is the slow heartbeat of the social organism, a vast systole and diastole of concentrating wealth and compulsive recirculation.” *Ibid*, p. 57.

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MATERNAL MORTALITY

The following case has been reviewed by the Colorado Maternal Mortality Committee* and selected for publication because of its educational value.

A 21-YEAR-OLD FEMALE GRAVIDA 2, para 0, aborta 1, whose estimated date of confinement was late November, 1974, had essentially no problems during her pregnancy with the exception of repeated complaints of pelvic pressure. All routine laboratory studies were within normal limits. There was no history of genito-urinary infection, blood pressures were normal, urine albumin was negative. Her past medical history included a spontaneous abortion.

The patient was first seen at approximately 36 weeks gestation for the possibility of premature labor. She was admitted for 24 hours, given 10 milligrams of Vasodilan orally four times a day, with cessation of labor. She was sent home on Vasodilan, 30 milligrams, three times a day. There was no evidence of urinary tract infection. Vasodilan was taken for one week after discharge.

She was next seen on November 22, 1974 for possible labor. Blood pressure was 135/90, however, the cervix was only one centimeter dilated and twenty per cent effaced, and she was given Vistaril and discharged. She was seen early on the 23rd of November. The cervix was unchanged and she was again sent home.

She was finally admitted in active labor later on November 23, 1974 with a cervical dilation of 5 centimeters, 80 per cent effaced, vertex at 0 station and membranes intact. Blood pressure ranged during labor, from 130/80 to 150/110. There was no proteinuria until a catheterized specimen was obtained five hours antepartum. Deep tendon reflexes were normal. She was treated with 3 grams of Mag-Sulfate intravenously, one gram per hour, which medication slowed her labor down requiring Pitocin augmentation. Although the first stage was somewhat prolonged, the second stage was only 10 minutes, and in the evening of November 23, she delivered a term male infant which had an APGAR of 8-9 and did well.

The patient's postpartum course was unremarkable. She remained afebrile, her hematocrit was 39 on her second postpartum day; Mag-Sulfate was discontinued after 24 hours. She was discharged on the third postpartum day with normal blood pressure, pulse and temperature. She was given prescription for Norinyl 1/50 and was instructed to begin taking it one week after discharge.

On December 10, 1974, she was found dead at home lying on a couch. She had not contacted or asked for any medical attention immediately prior to death.

Postmortem examination was performed which disclosed multiple pulmonary emboli, myometrial hypertrophy, and multiple extensive bland thrombi in the uterine and pelvic vessels. No microscopic evidence of endometritis was found. The cause of death was listed as multiple pulmonary emboli. There was no evidence of embolic disease in the legs.

The possibility that the prolonged labor associated with preeclampsia initiated some low grade disseminated intravascular coagulation process has to be considered in this case. Lactation suppressing medications were apparently not given to this patient although they could conceivably have influenced her increased ability to coagulate. Moreover, the oral contraceptive pills, had they been taken as directed, might have influenced the coagulation problem. This would suggest that perhaps the contraceptive pill should be given only after the six weeks postpartum visit instead of immediately postpartum as is currently the policy in several of the larger hospitals. It was the opinion of the Committee that this maternal death was probably not preventable.

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* The following physicians have been appointed to serve on the Maternal Mortality Committee, a subcommittee under Maternal and Child Health: Lawrence W. Roessing, Jr., Chairman; Maxwell A. Abelman, L. Joseph Butterfield, Watson A. Bowes, Jr., Horace E. Thompson, all of Denver; Bruce C. Richards, Lakewood; Mallory T. Harling, Fort Collins; Ronald E. Harrington, Boulder; James R. Patterson, Englewood; Edwin N. Running, Jr., Arvada; Louis C. Wollenweber, Jr., Lakewood; Thomas F. Purdon, Colorado Springs.

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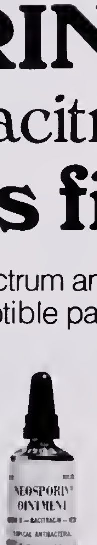

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Family Practice Program Accreditation

William Barrows, MD, Director of the Family Practice Residency training program in Pueblo, has announced that the three-year medical education program has been approved by the Liaison Committee on Graduate Medical Education on a provisional basis. Three years of residency education in the specialty of family practice, or family medicine, will be offered.

The program, whose offices and outpatient clinic are located in the Colorado State Hospital's General Hospital and Surgical building, is operated by the University of Colorado School of Medicine. It began operation on July 1, pending the outcome of the survey by the Residency Review Committee for Family Practice which was conducted several months ago. The Residency Review Committee, which is composed of representatives of the American Academy of Family Physicians, the American Board of Family Practice, and the AMA Council on Medical Education, has made its recommendations to the Liaison Committee.

Six resident doctors began their training in the program on July 1. They will be joined by six more next July 1 and an additional six in 1977, for a total of 18 who will be in training in the program at any one time thereafter. The trainees divide their training time between the clinic at the State Hospital and hospital training at St. Mary-Corwin and Parkview Episcopal hospitals.

Area Woman Elected To Institute

Patricia Rooney McAtee, assistant professor of pediatrics, University of Colorado School of Medicine, has been elected a member of the National Academy of Sciences' Institute of Medicine. Formerly an assistant professor of nursing, Ms. McAtee is the only woman from the Rocky Mountain Area who belongs to the 306-member institute; she is one of 39 female members.

A nationally known contributor to the field of health care and sciences, Ms. McAtee has developed an innovative national nurse practitioner program, endeavoring to expand the nurse's role to provide more meaningful, direct and responsible primary health care to patients.

The new Institute of Medicine member received her bachelor's degree from Loretto Heights College, Denver, and her master's from CU. She has been a member of the CU Medical Center faculty since 1961, beginning as an instructor in public health. She is chairperson of the national liaison committee, National Association of Pediatric Nurse Associates and Practitioners. An author or co-author of several articles, Ms. McAtee is on the board of directors of the Foundation for Urban and Neighborhood Development, Inc., Denver, and a former project director with the Western Interstate Commission for Higher Education. She belongs to the American Academy of Political and Social Scientists, Western Society for Research in Nursing, American Nurses' Association and the National League for Nursing.

Armstrong Receives Research Award

Donald Armstrong, MD, assistant professor, University of Colorado Department of Neurology, has been given a research professorship from the National Retinitis Pigmentosa Foundation, Inc., for $25,000 per year which may be extended for three years. Author or co-author of more than 45 publications, Doctor Armstrong will study particular enzymes found in the retina and pigment epithelium of dogs with retinal degeneration.

Doctor Armstrong received his bachelor's degree from San Diego State College, California, his master's from the CU Medical Center and his doctorate from the University of Tulsa, Oklahoma. He first came to CU in 1967 as an instructor of neurology. In 1970, he moved to Tulsa where he was an instructor of anatomy and physiology at Tulsa Junior College and director of the clinical research center at the Hillcrest Medical Center. He returned to UCMC in 1974.

He is a member of several professional organizations, including the International Federation of Clinical Chemistry, American Association of Clinical Chemists, Consulting Chemists Association, and the American Association for the Advancement of Science.

Neurosurgical Historian Named

Thomas K. Craigmile, MD, Denver neurosurgeon, has been named Historian for the Rocky Mountain Neurosurgical Society, Inc., while Michael J. McNally, MD, of Colorado Springs is a Member At Large.

The Immediate Past President is Michael Pollay, MD, of Albuquerque, New Mexico.

Gipson in Naval Program

Navy Medical Corps Lieutenant Bernard F. Gipson, Jr., a 1974 graduate of the University of Colorado School of Medicine, is currently enrolled in the Naval Flight Surgeon Program at the Naval Aerospace Medical Institute, Pensacola, Florida. Doctor Gipson is the son of Dr. and Mrs. Bernard F. Gipson, Sr., of Denver.

The Naval Flight Surgeon is a unique mixture of physician, flyer, scientist and naval officer. During the six month training course, Doctor Gipson will receive approximately 20 weeks of academic training followed by six weeks of flight training. Upon completion of the program, Doctor Gipson can expect to be assigned to an operational aviation unit of the Navy or Marine Corps.

THE
BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information. address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Recent Acquisitions

Acupuncture for Physicians: Teruo Matsumoto. Thomas, 1974. 204 p. $14.75.

A Common Sense Approach to Community Living Arrangements for the Mentally Retarded: John W. Fanning. Thomas, 1975. 95 p. Review copy. $8.50.

Congressional Staff Directory: Charles B. Brownson. 16th ed. Congressional Staff Directory, 1974. Gift of the Colorado Medical Society.

Colorado Staff Directory Advance Locator, 1975 Supplement. Congressional Staff Directory, 1975. Gift of the Colorado Medical Society.

The Doctor's Lawyer: Marc J. Lane. Thomas, 1974. 99 p. $12.75.

Evaluations of Drug Interactions—1973. American Pharmaceutical Association, 1973. 357 p. (With Supplement, 1974). $10.00.

The Future of Philanthropic Foundations: Symposium on the Future of Philanthropic Foundations. American Elsevier, 1975. 240 p. (Ciba Foundation Symposium, 30) 240 p. Gift.

The Law of Associations, an Operating Legal Manual for Executives and Counsel: George D. Webster. General Counsel of American Society of Association Executives, 1975. Various pagings. Gift.

The Medical Aspects of Sports: Timothy T. Craig, ed. American Medical Association, 1975. 64 p. Gift.

Medical Examination Review Book, Textbook Study Guide of Psychiatry: James R. Allen and Barbara Ann Allen. Medical Examination Publishing Co., Inc., 1975. Gift.

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Neurologic Infections in Children: William E. Bell. Saunders, 1975. (Major problems in clinical pediatrics, v. 12) 456 p. $19.80.

Parasites in the Immunized Host: Mechanisms of Survival: Symposium on Parasites in the Immunized Host. American Elsevier, 1974. (Ciba Foundation symposium, 25) 280 p. Gift.

The Pathology of Tumors: Lauren V. Ackerman and Juan Rosai. American Cancer Society, Inc., 1972. 55 p. Gift.

Symposium on Light-Coagulation, Argon Laser and Xenon Arc: Jules Francois. Williams and Wilkins, 1973. 95 p. $12.50.

Bonney's Gynaecological Surgery 8th Edition, by John Howkins and Sir John Stallworthy, Williams & Wilkins, 1974. 868 p. $37.75.

This classical work has been extensively, lovingly, indeed reverently reworked by two students of the master. In general terms, they have done an excellent job. The book is well illustrated, written in a conversational and highly readable style. The typical English understatement is quaint but effective (eg. "Self-abnegation should be the keynote of the first assistant"). Any practicing gynecologist could enhance his skill by carefully reading this text, and most medical students and house staff would find it basic enough to serve as a first step toward understanding the principles of gynecologic surgery.

The flaws are, for the most part, minor. The instruments and recommended medications are totally foreign to this reviewer (eg. the use of Hibitane for skin preparation). Many recommendations have fallen from general use in the United States (eg. shaving of the entire abdomen and vulva for all procedures, vaginal and abdominal). American surgeons may be surprised to find that "Silk sutures (are) seldom used". Inevitably, the reviewer's own experiences and prejudices come into conflict with the writers of any text. Condemnation of the marsupialization procedure of Bartholin duct cysts is a bit extreme. Likewise, the recommendation that three to five liters of carbon dioxide are required to perform laparoscopy is at variance with our experience.

Omissions are unavoidable in any general textbook. The failure to mention cervical cryosurgery, incidental suprapubic cystostomy, and any cervical cerclage procedures except the Shirodkar operation were obvious put probably justifiable oversights. However, one wonders, had the authors not devoted more than ten pages to the discussion of cervical amputation procedures, there would have been space for some of the more modern approaches to gynecologic conditions.

Particularly well done sections include those on radical vulvectomy, fistula repair, and of course, "Bonney's Operation", myomectomy. The recommendation that ovaries be conserved, prior to age forty-five, fortifies our opinion.

In summary, I enjoyed the book. It was a broadening and enriching experience to read one of the classics which has been kept reasonably up-to-date without losing the flavor of the original.

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AMERICAN ASSOCIATION
FOR THE STUDY OF HEADACHE AND
NATIONAL MIGRAINE FOUNDATION
DEPARTMENT OF NEUROLOGY
UNIVERSITY OF NEW MEXICO SCHOOL OF MEDICINE
SCRIPPS CLINIC AND RESEARCH FOUNDATION

CONTINUING EDUCATION IN PATHOGENESIS
AND TREATMENT OF

Headache

IN ADULTS AND CHILDREN

January 8, 9, 10, 1976,
Albuquerque, New Mexico

COURSE DIRECTORS: *Otto Appenzeller,* M.D., Ph.D., Editor, HEADACHE: *Donald J. Dalessio,* M.D., President, Am. Assn. for the Study of Headache; *Ruth Atkinson,* M.D., Director, Pediatric Headache Clinic, UNM School of Medicine

FACULTY: *Seymour Diamond,* Chicago; *Arnold Friedman,* Tucson; *John Graham,* Boston; *Lee Kudrow,* Encino; *Robert S. Kunkel,* Cleveland; *Robert Ryan Jr.,* Rochester; *Robert Ryan Sr.,* St. Louis; *Dewey Ziegler,* Kansas City; *Donald Dalessio,* La Jolla; *Otto Appenzeller, Ruth Atkinson, Thomas Carlow, A. Earl Walker,* all Albuquerque.

—18 LECTURES; 3 case presentations; 2 evening panels; afternoons free.

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MEETINGS

American Cancer Society-
National Cancer Institute

NATIONAL CONFERENCE ON CANCER RESEARCH AND CLINICAL INVESTIGATION

Hyatt Regency Atlanta Hotel, Atlanta, Georgia

September 20-22, 1976

Contact: American Cancer Society, Colorado Division, Inc., 1809 East 18th Avenue, Denver, Colorado 80218, or Call: (303) 321-2464.

American Academy for Cerebral Palsy

29TH ANNUAL MEETING

Fairmont Hotel, New Orleans, Louisiana

September 24-28, 1975

Contact: American Academy for Cerebral Palsy, 1255 New Hampshire Avenue, N.W. Washington, D.C. 20036.

Montrose Memorial Hospital

MONTROSE FALL CLINICS

Elk's Lodge, Montrose, Colorado

September 26-27, 1975

10 hours Credit: AAFP, ACGP

Contact: N. Robert Brethouwer, D.O., Chairman, Fall Clinics Committee, Montrose Memorial Hospital, Montrose, Colorado 81401.

University of Colorado School of Medicine,
Continuing Medical Education

BATTERED CHILD SEMINAR

September 29-30, 1975

Contact: Office of Postgraduate Medical Education, University of Colorado School of Medicine, 4200 East 9th Avenue, Denver, Colorado 80220.

New Mexico Department of
Hospitals and Institutions

THE MENTALLY RETARDED IN THE COMMUNITY

Hilton Inn, Albuquerque, New Mexico

September 30-October 1, 1975

Contact: Carole Gorney, Los Lunas Hospital and Training School, P.O. Box 208, Los Lunas, New Mexico 87031.

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Frisco Pharmacy—Colorado Mountain College
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ENVIRONMENTAL MEDICINE
SYMPOSIUM

Holiday Inn, Frisco, Colorado

October 5, 1975

Contact: "Bo" Bogan, 418 Main Street, Frisco, Colorado 80443, or call: (303) 468-6858.

New Mexico State Medical Society

EMERGENCY MEDICAL SERVICES SEMINAR

Holiday Inn-Midtown, Albuquerque,
New Mexico

October 8, 1975

Contact: George W. Dunham, P.O. Box 1293, Albuquerque, New Mexico 87103.

Montana Medical Association

97TH ANNUAL MEETING

Ramada Inn, Butte, Montana

October 9-11, 1975

American College of Physicians

THE CLINICAL SPECTRUM
OF ADULT HEART DISEASE

University of New Mexico
School of Medicine, Albuquerque,
New Mexico

October 16-18, 1975

Contact: Registrar, Postgraduate Courses, ACP, 4200 Pine St., Philadelphia, Pennsylvania 19104.

American College of Gastroenterology

COURSE IN PRACTICAL
CLINICAL GASTROENTEROLOGY

The Hilton, Las Vegas, Nevada

October 22-23, 1975

Contact: American College of Gastroenterology, 299 Broadway, New York City, New York 10007.

Albuquerque Cardiovascular Associates, Ltd.

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INTERPRETATION FOR THE CLINICIAN

Presbyterian Hospital Center,
Albuquerque, New Mexico

October 23-25, 1975

Contact: Barry W. Ramo, MD, 201 Cedar S.E., Suite 604, Albuquerque, New Mexico 87106.

Rondomycin®
(methacycline HCl)

CONTRAINDICATIONS: Hypersensitivity to any of the tetracyclines.
WARNINGS: Tetracycline usage during tooth development (last half of pregnancy to eight years) may cause permanent tooth discoloration (yellow-gray-brown), which is more common during long-term use but has occurred after repeated short-term courses. Enamel hypoplasia has also been reported **Tetracyclines should not be used in this age group unless other drugs are not likely to be effective or are contraindicated.**
Usage in pregnancy. (See above **WARNINGS** about use during tooth development.)
Animal studies indicate that tetracyclines cross the placenta and can be toxic to the developing fetus (often related to retardation of skeletal development). Embryotoxicity has also been noted in animals treated early in pregnancy
Usage in newborns, infants, and children. (See above **WARNINGS** about use during tooth development)
All tetracyclines form a stable calcium complex in any bone-forming tissue A decrease in fibula growth rate observed in prematures given oral tetracycline 25 mg/kg every 6 hours was reversible when drug was discontinued
Tetracyclines are present in milk of lactating women taking tetracyclines.
To avoid excess systemic accumulation and liver toxicity in patients with impaired renal function, reduce usual total dosage and, if therapy is prolonged, consider serum level determinations of drug The anti-anabolic action of tetracyclines may increase BUN While not a problem in normal renal function, in patients with significantly impaired function, higher tetracycline serum levels may lead to azotemia, hyperphosphatemia, and acidosis.
Photosensitivity manifested by exaggerated sunburn reaction has occurred with tetracyclines Patients apt to be exposed to direct sunlight or ultraviolet light should be so advised, and treatment should be discontinued at first evidence of skin erythema.
PRECAUTIONS: If superinfection occurs due to overgrowth of nonsusceptible organisms, including fungi discontinue antibiotic and start appropriate therapy.
In venereal disease, when coexistent syphilis is suspected, perform darkfield examination before therapy, and serologically test for syphilis monthly for at least four months.
Tetracyclines have been shown to depress plasma prothrombin activity; patients on anticoagulant therapy may require downward adjustment of their anticoagulant dosage.
In long-term therapy, perform periodic organ system evaluations (including blood, renal, hepatic).
Treat all Group A beta-hemolytic streptococcal infections for at least 10 days.
Since bacteriostatic drugs may interfere with the bactericidal action of penicillin, avoid giving tetracycline with penicillin.
ADVERSE REACTIONS: **Gastrointestinal** (oral and parenteral forms), anorexia, nausea, vomiting, diarrhea, glossitis, dysphagia, enterocolitis, inflammatory lesions (with monilial overgrowth) in the anogenital region
Skin: maculopapular and erythematous rashes; exfoliative dermatitis (uncommon). Photosensitivity is discussed above (See **WARNINGS**)
Renal toxicity: rise in BUN, apparently dose related (See **WARNINGS**)
Hypersensitivity: urticaria, angioneurotic edema, anaphylaxis, anaphylactoid purpura, pericarditis, exacerbation of systemic lupus erythematosus
Bulging fontanels, reported in young infants after full therapeutic dosage, have disappeared rapidly when drug was discontinued
Blood: hemolytic anemia, thrombocytopenia, neutropenia, eosinophilia
Over prolonged periods, tetracyclines have been reported to produce brown-black microscopic discoloration of thyroid glands; no abnormalities of thyroid function studies are known to occur
USUAL DOSAGE: **Adults**—600 mg daily, divided into two or four equally spaced doses. More severe infections an initial dose of 300 mg followed by 150 mg every six hours or 300 mg every 12 hours. Gonorrhea In uncomplicated gonorrhea, when penicillin is contraindicated, Rondomycin' (methacycline HCl) may be used for treating both males and females in the following clinical dosage schedule 900 mg initially, followed by 300 mg q i d for a total of 5 4 grams
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Therapy should be continued for at least 24-48 hours after symptoms and fever have subsided
Concomitant therapy: Antacids containing aluminum, calcium or magnesium impair absorption and are contraindicated Food and some dairy products also interfere Give drug one hour before or two hours after meals Pediatric oral dosage forms should not be given with milk formulas and should be given at least one hour prior to feeding
In patients with renal impairment (see **WARNINGS**), total dosage should be decreased by reducing recommended individual doses or by extending time intervals between doses
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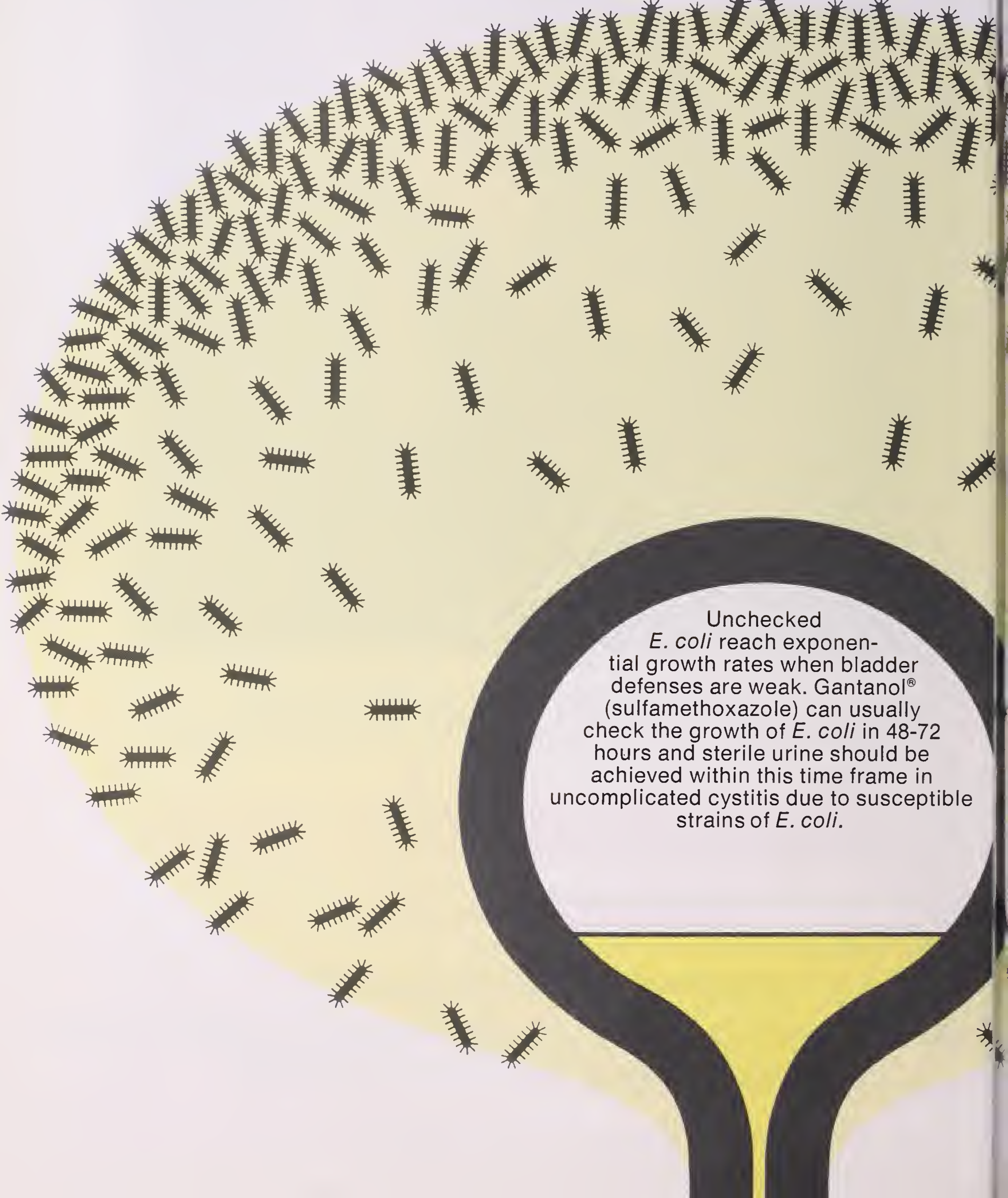

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Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. ***Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* WARNING
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 capsules; in Single Unit Packages of 100 (intended for institutional use only).

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Just once or twice daily for maintenance.
Hydrochlorothiazide to help keep blood pressure down and triamterene to help keep potassium levels up.

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Warnings: Patients with severe cardiac disease should be given this medication with caution. Fever and possibly heat stroke may occur due to anhidrosis.

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Overdosage should be avoided in patients severely ill with ulcerative colitis.

Adverse Reactions: Varying degrees of drying of salivary secretions may occur as well as mydriasis and blurred vision. In addition the following adverse reactions have been reported: nervousness, drowsiness, dizziness, insomnia, headache, loss of the sense of taste, nausea, vomiting, constipation, impotence and allergic dermatitis.

Dosage and Administration: The recommended daily dosage for adult oral therapy is one 15-mg. tablet with meals and two at bedtime. Subsequent adjustment to the patient's requirements and tolerance must be made.

How Supplied: Pro-Banthīne is supplied as tablets of 15 and 7.5 mg., as prolonged-acting tablets of 30 mg. and, for parenteral use, as serum-type vials of 30 mg.

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Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration

The idea of a so-called patient package insert has been around for a long time. Many physicians alread use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

Dr. James H. Sammons
Executive Vice President
of the American
Medical Association

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

ain purpose of drug information r the patient is to get his coopera- on in following a drug regimen.

eparation and distribution of itient drug information

We would hope to amass infor- ation from physicians, medical ocieties, the pharmaceutical indus- y and centers of medical learning. ne ultimate responsibility for uni- rm labeling must, however, rest ith the Food and Drug Administra- on. There is nothing wrong with is agency saying, "this informa- on is generally agreed upon and erefore it should be used," as long our process for getting the infor- ation is sound.

Distribution of the information a problem. In great measure it ould depend on the medication in uestion. For example, in the case an injectable long-acting proges- erone, we would think it mandatory issue two separate leaflets—a hort one for the patient to read be- ore getting the first shot and a long ne to take home in order to make a ecision about continuing therapy. this case, the information might e put directly on the package and ot removable at all. But for a medi- ation like an antihistamine this formation might be issued sepa- ately, thus giving the physician the ption of distribution. This could reserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socio-economic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

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nly the doctor can remove that fear y 20 or 30 minutes of conversation.

I'm not suggesting that we ithhold any information from the atient because, first of all, it would e totally dishonest and secondly, it ould defeat the very purpose of the nsert. I do think that a patient on the irth control pill should know about he incidence of phlebothrombosis.

If you're going to tell a patient he incidence of serious adverse re- ctions, then you have to tell him hat a concerned medical decision was made to use a particular medi- cation in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequenc and/or severity of grand mal seizures ma require increased dosage of standard anti convulsant medication; abrupt withdrawa may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and mus cle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

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in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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OUR COVER

Both Visit to Yesterday and exploration of unparalleled Southwestern Colorado vistas, the route of the Denver Rio Grande and Western narrow gauge railroad along the Animas River as it goes from Durango to Silverton and return is always enthralling. Bob Miller captures the excitement of the journey in this one of many of his fine photos the Journal has been privileged to use.

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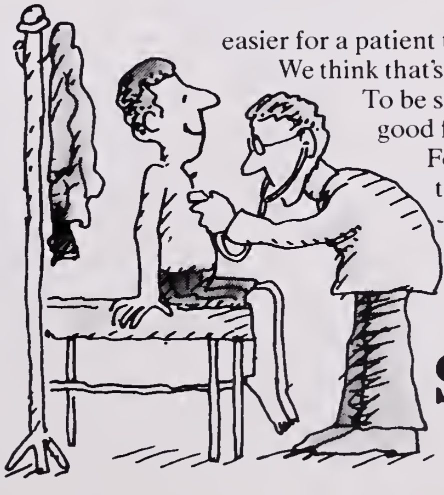

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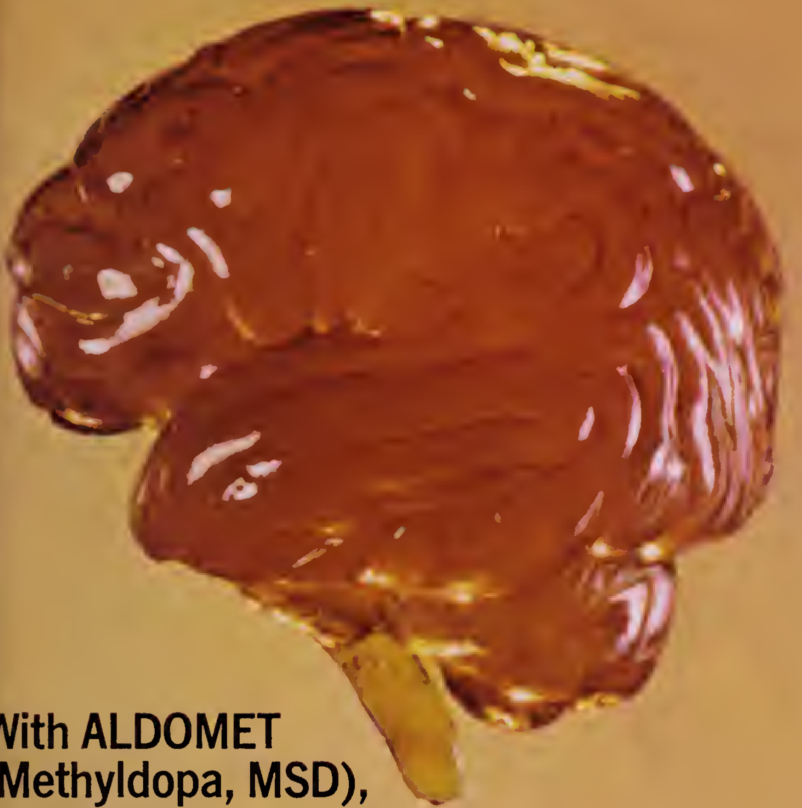

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Contraindications: Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reaction or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites. Stop drug if involuntary choreoathetotic movement occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses o anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patient on methyldopa because the drug is removed by thi procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usuall early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, involuntar choreoathetotic movements; psychic disturbances including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa i edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness o mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, skin rash.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

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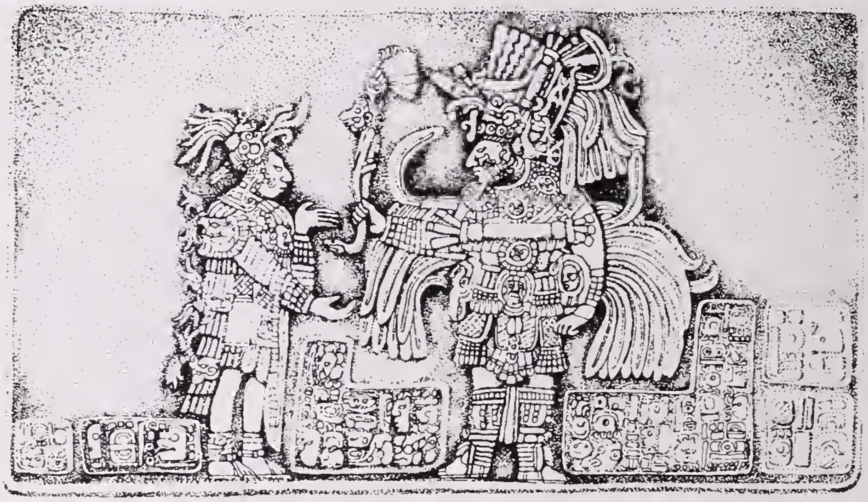

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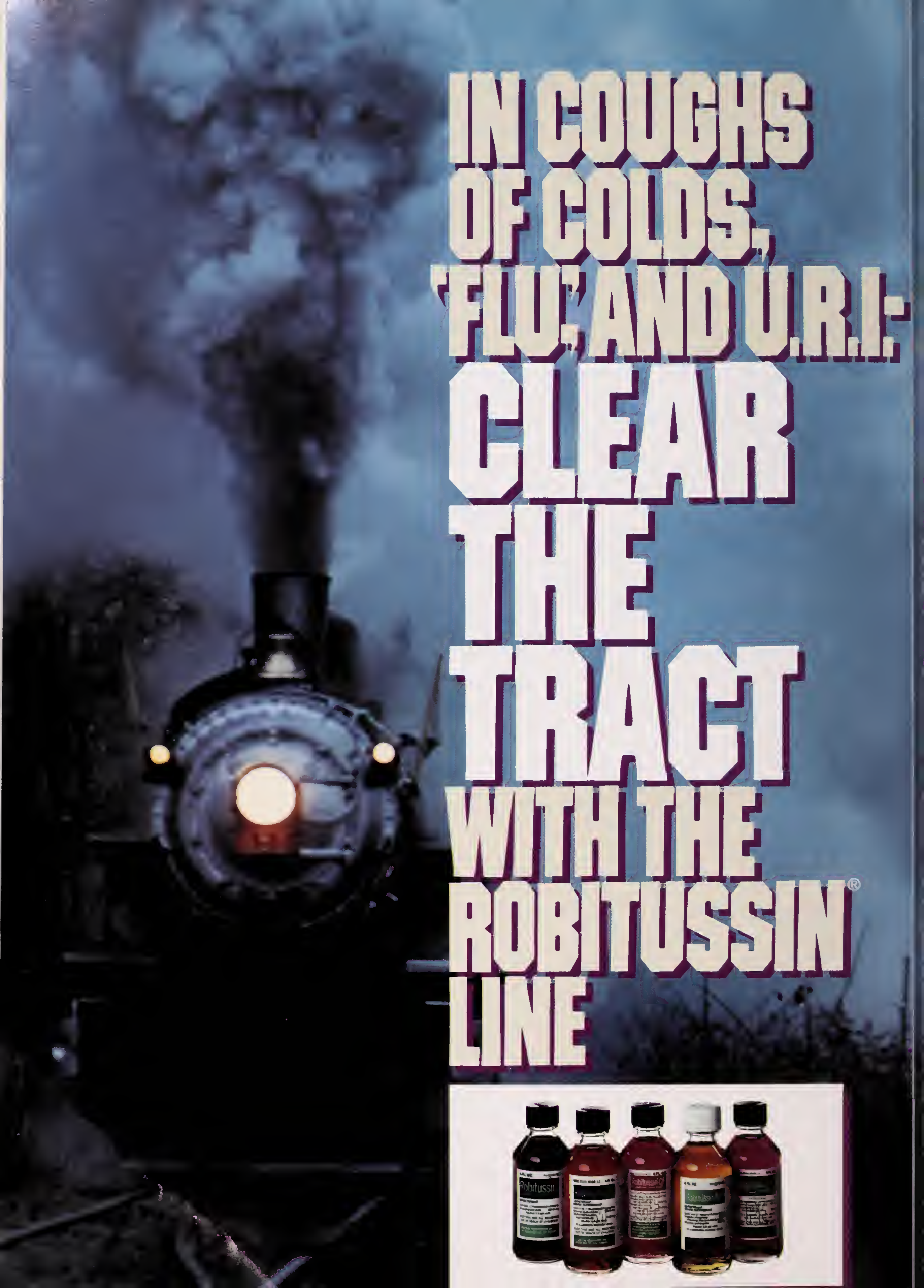
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WITH THE ROBITUSSIN® LINE
Robitussin

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★formerly named Glyceryl Guaiacolate

For productive and unproductive coughs

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Each 5 ml teaspoonful contains:

Guaifenesin, NF	100 mg
Alcohol, 3.5%	

For severe coughs

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Each 5 ml teaspoonful contains:

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Non narcotic for 6-8-hr. cough control

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Dextromethorphan Hydrobromide, NF	15 mg
Alcohol, 1.4%	

Decongests nasal passages and sinus openings as it helps relieve coughs

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Guaifenesin, NF	100 mg
Pseudoephedrine** Hydrochloride, NF	30 mg
Alcohol, 1.4%	
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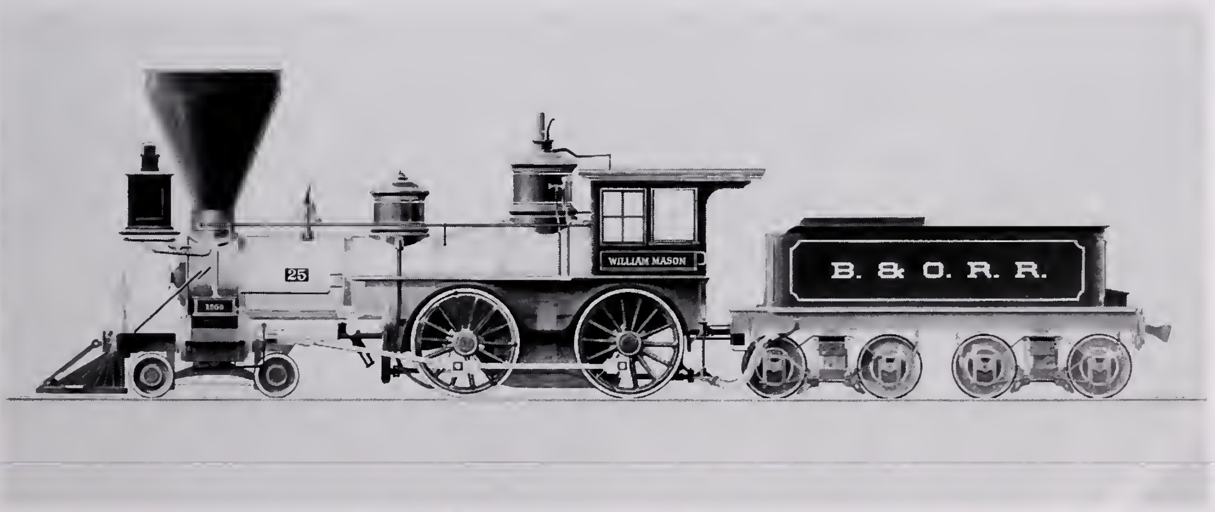

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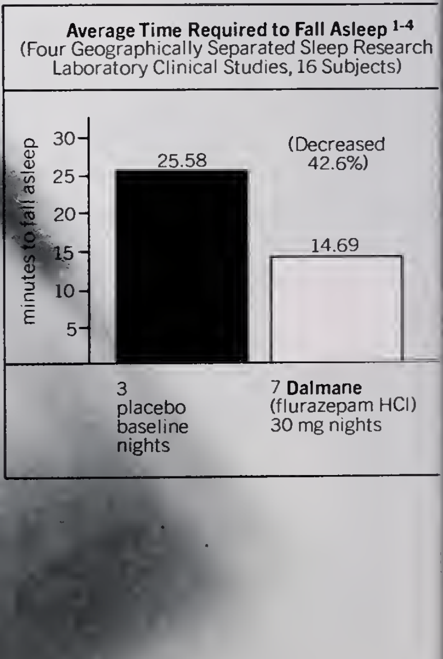
As demonstrated below, Dalman induces sleep within 17 minutes, on average:[1-4]



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…sleep research laboratory clinical studies prove: Dalmane decreases number of nighttime awakenings and increases total sleep time.[5]

Dalmane (flurazepam HCl) is relatively safe, seldom causes morning "hang-over"

Dalmane is generally well tolerated. The usual adult dose of 30 mg should initially be lowered to 15 mg for the elderly and debilitated, to help preclude oversedation, dizziness or ataxia. Appraisal of possible risks is suggested before prescribing.

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3. Vogel GW: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
4. Dement WC: Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ
5. Data on file, Medical Department, Hoffmann-La Roche Inc., Nutley NJ

Before prescribing Dalmane (flurazepam HCl), please consult complete product information, a summary of which follows:

Indications: Effective in all types of insomnia characterized by difficulty in falling asleep, frequent nocturnal awakenings and/or early morning awakening; in patients with recurring insomnia or poor sleeping habits; and in acute or chronic medical situations requiring restful sleep. Since insomnia is often transient and intermittent, prolonged administration is generally not necessary or recommended.

Contraindications: Known hypersensitivity to flurazepam HCl.

Warnings: Caution patients about possible combined effects with alcohol and other CNS depressants. Caution against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving). Use in women who are or may become pregnant only when potential benefits have been weighed against possible hazards. Not recommended for use in persons under 15 years of age. Though physical and psychological dependence have not been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage.

Precautions: In elderly and debilitated, initial dosage should be limited to 15 mg to preclude oversedation, dizziness and/or ataxia. If combined with other drugs having hypnotic or CNS-depressant effects, consider potential additive effects. Employ usual precautions in patients who are severely depressed, or with latent depression or suicidal tendencies. Periodic blood counts and liver and kidney function tests are advised during repeated therapy. Observe usual precautions in presence of impaired renal or hepatic function.

Adverse Reactions: Dizziness, drowsiness, lightheadedness, staggering, ataxia and falling have occurred, particularly in elderly or debilitated patients. Severe sedation, lethargy, disorientation and coma, probably indicative of drug intolerance or overdosage, have been reported. Also reported were headache, heartburn, upset stomach, nausea, vomiting, diarrhea, constipation, GI pain, nervousness, talkativeness, apprehension, irritability, weakness, palpitations, chest pains, body and joint pains and GU complaints. There have also been rare occurrences of leukopenia, granulocytopenia, sweating, flushes, difficulty in focusing, blurred vision, burning eyes, faintness, hypotension, shortness of breath, pruritus, skin rash, dry mouth, bitter taste, excessive salivation, anorexia, euphoria, depression, slurred speech, confusion, restlessness, hallucinations, and elevated SGOT, SGPT, total and direct bilirubins and alkaline phosphatase. Paradoxical reactions, *e.g.*, excitement, stimulation and hyperactivity, have also been reported in rare instances.

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Economy Dictates

Beginning January 1976 the *Rocky Mountain Medical Journal* will be published every other month by action of its Editorial Board at its annual meeting in September 1975. Although the financial statement for the *Journal* and the Directory for the past fiscal year shows a positive balance, the solvency of the operation was marginal. Erosion of this sound economic position by continuing inflation and proposed increase in mailing costs dictated the action.

Every type publication over the past several years has been confronted with the same economic pressures. Each has attempted to modify its operation to adjust to the situation. Some have folded. Our solution principally has been to reduce editorial content by about forty per cent. We have also changed the printing format and have attempted to increase our income from local advertising.

A fundamental problem for most medical journals has been a decrease in national advertising by the pharmaceutical companies—who have their own government-aggravated economic problems. However, the *Journal* has been assured of essentially the same yearly support by our national advertisers with publication every other month. Therefore, the editorial portion of each bimonthly issue can be almost twice the present size, but there will be savings on mailing and printing.

Otherwise we plan no major changes in format or policy. However, because the scientific and literary quality of submitted papers has improved significantly over the past few years, because the number of presented papers steadily increases and because our editorial volume is less than it was several years ago, the editors must necessarily be more discriminating in selection for publication. There will be less emphasis on area and specialty representation, but, as compensation, the scientific caliber of the *Journal* will continue to improve. There shall continue to be a yearly issue featuring articles from each of our participating states.

We believe that you, our readership, recognize the financial problems and will appreciate the decision of the Board to remain solvent by these economizing actions. We know you will be pleased with an overall improvement in the scientific caliber of the *Journal.*

The Liability Challenge

Every medical journal in America somewhere in its editorial content addresses the problem of professional liability insurance. Surely everything has been said. The liability insurance situation is the nation's most critical current dilemma in health care—for the doctor and for the patient. We have neither new information nor new solutions. But we must continue to speak to the problem because there are too many Americans who do not yet appreciate the significance of the issues. That our impact is probably of little consequence does not absolve our responsibility to inform whenever we can.

Discussion of whether there be a crisis in any specific state or area is an exercise in semantics. By any name, that there have been area work stoppages because of unavailability of insurance, that premiums are everywhere already too high and in some places impossible, that able physicians are quitting practice or changing to non-contact work, that respected medical institutions face bankruptcy, that there is probability of unavailability of insurance in some states and regions, point to a situation which threatens the foundation of our system of medical care. The health and lives of the American people is at issue. The ultimate loser is the patient because he is the recipient of the available medical care and he is stuck with most of the increased cost. The magnitude of the problem is obvious to anyone who considers it.

Moreover, to attempt to solve the problem without recognizing as the basic cause the change in moral philosophy of Americans, is to avoid reality. Granted, the doctor-patient relationship has been strained by increasing specialization and increasing impersonalization of modern medical care. But the fact is that health care in America is the best in the world, and the fact is that the knowledge and capability of the American physician is uniformly better, with more consistent and uniform peer supervision, than ever before. The basis of the problem is that it is apparently morally acceptable for a person to acquire money by any means short of armed robbery, kidnaping, or murder. This change in moral standards and the modern political atmosphere of emphasis on misjudgement and error has produced the climate for the avalanche of malpractice claims. Thus we can understand why the able physician has been more vulnerable than the bad apple. Thus we can explain the epidemic of claims in Cook County (one of every five doctors is being sued) in the interval between legislative passage of a bill to curtail malpractice litigation and the governor's signature to make it a law.

Of course there are many contributing causes for the problem in medical liability. Our intent is not to oversimplify the issue. Rather, our purpose is to identify the basic cause—because it must be joined. Governments are necessary because people are not perfect. Although we can work and hope for change in the moral climate of our world, we must solve our immediate problem by legislation. Each of us must explain the problem and the urgency to his legislator. Today!

Hope for SIDS

Infant mortality in the United States dropped to 15.3 per 1000 live births in May of 1975, the lowest in history. However, some forms of infant death remain both enigmatic and unreported. One of these is Sudden Infant Death Syndrome (SIDS). Seventy-two infant deaths were signed out as SIDS in Colorado in 1974. With 38,700 live births during that year, and an incidence of three per 1000 live births, we estimate that 116 babies actually died with SIDS.

Vigorous educational efforts by the Colorado Chapter of the National Foundation for Sudden Infant Death has stimulated the reporting of SIDS, and relieved the anxiety of anguished parents. Until all cases are reported for establishment of epidemiologic trends, and until all families are properly supported by relatives, friends, and officials—in addition to their family physician—both the enigma of SIDS as a disease, and the parental pain will continue. The Colorado legislature has been petitioned to require a mandatory autopsy on all infant deaths under one year of age in the Medical Examiner reform bill.

These educational and legislative attacks on a major public problem are encouraging events.

L. Joseph Butterfield, MD
The Children's Hospital, Denver

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DENVER MEDICAL SOCIETY

TUESDAY, OCTOBER 28, 1975

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Computerized transaxial tomogram

Relationship to other neurodiagnostic procedures

Frederick T. Boulware, Jr., MD, Las Vegas, Nevada*

The technic of Computerized Transaxial Tomography, revolutionary in terms of the information it provides, can be used to best advantage when understood in relation to other neurodiagnostic procedures.

A COMPUTERIZED TECHNIC of evaluating the brain has been described.[1,2] The commonly used term for this new technic is computerized (trans) axial tomography. The Computerized Transaxial Tomogram (CTT) is sometimes simply referred to by the trade name EMI-Scan, or as at our center, the Computerized Neuro-Scan.

The CTT is the most revolutionary advance in diagnostic neurology in many years. Our preliminary experience echoes the enthusiasm which now seems universal among those charged with the responsibility of evaluating the neurologic patient.

The informational output of the CTT is basically applied neuroanatomy through visualization of the parenchyma, ventricular system, and portions of the subarachnoid spaces. It permits the unique opportunity to correlate neuroanatomy and neuropathology with an understanding of neurophysiology. This communication will briefly review this neurodiagnostic technic and its relationship to other procedures in diagnostic neurology.

Procedure

The procedure involves the use of narrow x-ray beams which pass through the patient's head and are detected by two sodium iodine crystals that always remain aligned with the source beam. Each crystal detects one-half of the beam. The head is scanned linearly with each detector recording 240 photon transmissions. The gantry (common housing for the x-ray source and detectors) is rotated one degree and the process repeated in the same plane. This one degree rotation is continued for 180° for a total of 43,200 readings. The computer then calculates a total of 25,600 absorption values for each picture point of the 160 by 160 matrix. The informational output is seen as a numerical printout representing the different tissue densities, or it can be read from a cathode ray oscilloscope in which shades of gray reproduce the neuroanatomical details. The routine series of scans requires up to 30 minutes to perform.

The data obtained provides cross-sectional views of the brain, ventricular system, portions

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*Dr. Boulware is the Director, Computerized Neuro-Scan Center, Las Vegas, Nevada 89109.

TABLE 1

A partial list of symptoms potentially requiring CTT evaluation.

- Headache
- Seizures
- Limb and/or facial weakness
- Incoordination
- Gait disturbances
- Altered states of consciousness
- Personality/intellectual changes
- Altered facial and/or limb sensation
- Visual disturbances
- Hearing loss
- Vertigo
- Speech or language difficulties

This test may be performed in the asymptomatic individual with proven malignancy with a potential of central nervous system metastasis.

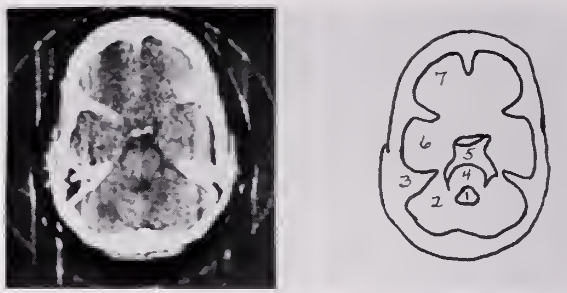

Fig. 1. An example of a single normal scan taken at a low level showing: 1) fourth ventricle; 2) cerebellar hemispheres; 3) petrous bones; 4) pons; 5) subarachnoid space; 6) temporal lobes; and 7) frontal lobes.

of the subarachnoid spaces, and skull. These results potentially can define altered densities of the bone or brain as well as show any alteration in the configuration of the ventricular system or any of its parts.

Clinical application

A partial list of symptoms, the nature of which may be clarified by the CTT, is seen in Table 1. When combined with the history, neurological examination, and physiologic data of electroencephalography, the structural information provided by the CTT is more detailed than was previously possible, short of using the potentially more hazardous procedures of angiography and pneumoencephalography.

To assess the value of this technic, it should be compared with the five other major studies used to assess disorders involving the brain, namely, cerebral angiography, radioisotope brain scan, pneumoencephalography, echoencephalography, and electroencephalography.

Angiography permits the delineation of the status of the vasculature in the neck as well as within the cranium. It demonstrates disturbances which alter the vascular pattern within the head. This technic remains the most definitive means of delineating the status of the carotid arteries in the neck regarding stenosis or occlusion, and it is the most definitive test in determining the presence or absence of intracranial aneurysms. Angiography oftentimes best demonstrates the presence of subdural hematoma. Contrariwise, epidural and intracerebral hematoma are readily detected by the CTT. Arteriovenous malformation may be detected by angiography depending upon the size of the malformation. Non-calcified vascular malformations could possibly be missed by the CTT unless intravenous contrast media is used. Angiography may disclose the presence of a mass lesion and its relative vascularity, but the CTT may demonstrate such lesions at an earlier stage than angiography. CTT may, therefore, disclose lesions which may or may not cause alteration of the vascular patterns, and when some of these lesions do cause an alteration of the vascular patterns, they may be disclosed at an earlier stage or at a time when the angiogram is negative. It should be emphasized, however, that after initial screening with the CTT, further study with angiography may be needed before any surgical procedure is performed. CTT has the added advantage of harboring no risk to the patient.

Radioisotope brain scan involves the intravenous injection of radioisotope material which can be scanned immediately upon the injection in a way to assess the initial passage of the radioisotope through the cranium and also some two hours following the injection. The procedure depends upon the alteration of cerebrovascular permeability, and may define relatively vascular neoplasms, brain abscess, or subdural hematoma. The CTT, however, is more precise than the brain scan in defining intracranial structural lesions, since permeability may not have been altered. For example, in patients who have suffered a vascular occlusion with infarction, the CTT may be positive within 24 hours subsequent to infarction, whereas the radioisotope brain scan will usually not show increased uptake up to one week following the event. The CTT not uncommonly demonstrates an intracranial mass lesion, such as a neoplasm, in the presence of a normal radioisotope brain scan. CTT is superior to this technic in defining the presence or absence of metastatic lesions. In

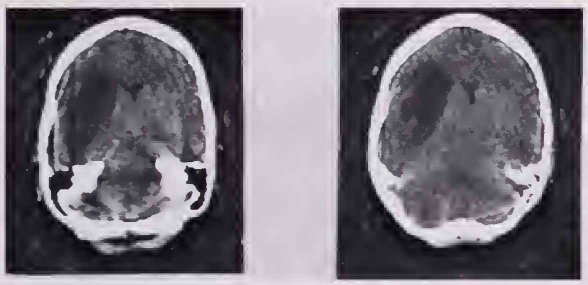

Fig. 2. A low grade glioma of the left temporal lobe in a 38-year-old female who presented with an isolated and generalized major motor episode. The neurological examination and a radioisotope brain scan were normal.

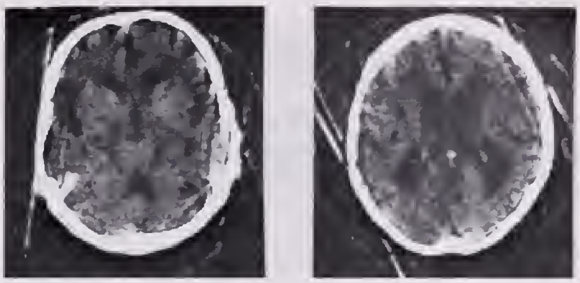

Fig. 3. Cerebral atrophy in a 75-year-old male with dementia. Note the dilatation of the ventricular system and increase in the subarachnoid space.

some centers when treatment for a primary tumor with a potential for metastasis to the central nervous system is being considered (i.e. lung, breast), the CTT is used to ascertain whether such metastasis has in fact occurred, and this may have implications for the mode of treatment.[3] Furthermore, the radioisotope brain scan provides no information regarding the ventricular system or those tumors which do not alter vascular permeability, as is frequently the case in low grade gliomas. There is also frequent difficulty in assessing the possibility of a structural lesion in the posterior fossa with the radioisotope brain scan. The CTT provides excellent visualization of this region.

Pneumoencephalography employs the lumbar injection of air into the subarachnoid space and offers the ability to outline the ventricular system as to its size or the presence or absence of a block or deformity of the ventricular system by a mass lesion. The major difficulties in the use of the procedure are the usual considerable discomfort experienced by the patient and the possible complications, such as deterioration in patients with senile dementia or subdural hematoma. Such complications can be avoided by the CTT. The CTT permits delineation of the ventricular system and permits one to evaluate its size, configuration, and as mentioned, furnishes information about the underlying pathology, without any risk or discomfort to the patient.

Echoencephalography is a simple study associated with no discomfort to the patient which, however, provides limited information. It assesses only the relative size and possible shift of the usual midline third ventricle. It may demonstrate enlargement of the third ventricle or a shift of this structure. The CTT, however, provides far more definitive information regarding not only the third ventricle, but the entire ventricular system, as to its size or displacement, and furnishes additional information about the underlying structural pathology.

Electroencephalography, like the CTT, is also painless and safe for the patient. It permits assessment of cortical function and at times indicates in an indirect manner disorders originating subcortically or in the posterior fossa. Electroencephalography, however, is in a category different from all of the procedures mentioned previously because it alone is based upon physiologic assessment. Electroencephalography, therefore, is the only procedure capable of assessing the possibility of a metabolic condition causing alterations in mentation as well as remaining the definitive test in patients with episodes of altered awareness in which there is a question of a seizure disorder. Its role then, should be adjunctive to that of the CTT.

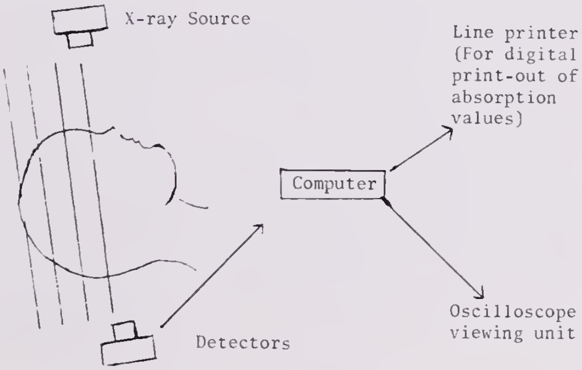
X-ray Source
Line printer (For digital print-out of absorption values)
Computer
Oscilloscope viewing unit
Detectors

Fig. 4. Schematic diagram representing the basic principle in obtaining a CTT using the EMI-Scanner. The x-ray source and the aligned detector crystals rotate around the patient's head. The computer receives the data and the calculated absorption values are printed in numerical form, and can also be viewed on the oscilloscope with the brightness being proportional to the values obtained for each point.

Summary

The CTT is a safe and accurate diagnostic tool which complements the physiologic data of central nervous system function currently available by electroencephalography. It easily can be done on an out-patient basis. It reduces the need for angiography, pneumoencephalography, and radioisotope brain scan. In addition, this procedure allows more precise definition of not only the brain parenchyma, but also the ventricular system. •

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4-6-8-10-12-75

Team management of the burned child

Ann M. Kosloske, MD, and Associates*, Denver

Resuscitation, wound care, and rehabilitation of a child with a major burn requires a specialized team.

MAJOR BURNS IN CHILDREN remain a significant cause of hospitalization, disfigurement, and death. The diverse problems associated with a catastrophic burn in a child require time and expertise beyond the capability of a single surgeon, however skillful and dedicated. In our institution a "burn team" was formed, consisting of a pediatric surgeon, pediatrician, orthopedist, plastic surgeon, nurse, psychologist, social worker, physiotherapist, and occupational therapist. The Shriner's Burns Institute, Galveston Branch, provided special training and inspiration. Our current guidelines for resuscitation, wound care and rehabilitation are reviewed with reference to a child who survived a 75 per cent burn.

CASE REPORT

A 17-month-old adopted white girl was admitted to the Children's Hospital of Denver with a 75 per cent burn. She had pulled over a bucket of extremely hot tap water and had fallen into it, and contact with skin had been prolonged. She reached the Emergency Room 35 minutes after the accident.

Physical examination disclosed a listless but conscious child with burns involving the right half of the head and anterior trunk, both arms, entire back and right leg. Rectal temperature was 95.4F, pulse 168, blood pressure 50 systolic, weight 7.5 kg.

Resuscitation was begun with percutaneous passage of a subclavian central venous catheter and rapid administration of lactated Ringer's solution in 5 per cent dextrose, followed by electrolyte-albumin solution (Table 1). Urinary catheter and nasogastric tube were introduced. Temperature was gradually restored to normal by means of a radiant heat lamp and warming mattress. Blood pressure rose, and the patient was transiently hypertensive with pressure as high as 130-140/90 in the first 12 hours. Urinary output was adequate at 10-20 cc/hour, despite specific gravities as high as 1.030, with glycosuria. Tetanus toxoid and intravenous penicillin were administered.

After 12 hours, the nasogastric tube was removed and hourly feedings of milk and a high caloric diet were begun, which the child tolerated well. Stools were occasionally positive for occult blood, but she did not develop significant gastrointestinal hemorrhage. At 36 hours, edema was excessive, and small doses of intravenous furosemide were administered. Diuresis began and was sustained over the next several days.

The burn wound was cleansed, debrided, and dressed with silver sulfadiazene. Approximately two-thirds of the burned area (50 per cent of total body surface) was full thickness injury. Daily bathing in a dilute sodium hypochlorite solution, followed by debridement, and reapplication of silver sulfadiazene dressings, was carried out. Because of restrictive edema of the hands, bilateral escharotomy was performed, with a linear incision extending along the dorsum of the hand and distal third of the forearm. Tangential excision of burn eschar was performed at 6, 12, and 14 days, followed by application of porcine heterograft. Autografting, utilizing meshgraft and re-use of the limited donor sites ("re-harvesting") was done at 12, 22, 28, 36, and 46 days.

TABLE 1

Composite Burn Solution

920 ml	D 2 1/2 in 1/2 normal saline
50 ml	25% human serum albumin
20 ml	Na bicarbonate (1mEq / ml)
10 ml	hypertonic NaCl (3mEq / ml)
1000 ml	

---

*Associates from The Burn Team of the Children's Hospital, Denver, are James K. Todd, MD; Robert Horner, MD; William E. Powers, MD; Chester Poremba, PhD; Janet K. Buttrick, RN; Lou Shannon, RPT; Ann Grady, OTR, and Helen Hondius, MSW.

There were no episodes of sepsis. Systemic antibiotics were begun on one occasion, when hypothermia and anorexia suggested sepsis, but were discontinued three days later when cultures were negative. Marked improvement in temperature control, as well as a return of normal social responses to her environment, accompanied coverage of the burn wound with skin grafts.

Skeletal traction was employed for 30 days to all four extremities and all ten fingers. Range of motion exercises were performed several times daily. Traction was removed after grafts had "taken," and splints were utilized to prevent contracture during the healing phase. There was sustained and meticulous attention to prevention of contracture by the physical therapy and occupational therapy staff. Splints and elastic supports were utilized. Function was excellent.

The parents received additional support and guidance throughout the course from the psychologist and social worker. The child was discharged on the 81st post-burn day. A long followup by the "burn team" is anticipated.

Discussion

Mortality of a 75 per cent burn, two-thirds of which is full thickness, in a 17-month-old child, approximates 90 per cent.[1] Management may be considered in three phases: resuscitation, wound care and rehabilitation.

Resuscitation

Resuscitation requires rapid assessment of the extent and depth of burn and evaluation of the patient's airway and peripheral circulation. Associated injuries must be looked for.

Monitoring is begun immediately. Blood pressure measurements are possible, even in burned extremities, employing the Doppler instrument over a layer of sterile gauze or sheet wadding. A urinary catheter is necessary for hourly measurements of volume, which should be 1-2 cc/kg/hr, and specific gravity, which should be less than 1.025. Since burned children are prone to hypothermia, temperature monitoring is begun immediately; a warming mattress or radiant heat lamp is often necessary. The patient is weighed on the same scale on which daily weights will be taken.

A large-bore venous cannula is placed through a surgically prepared area, (unburned skin if available) either percutaneously or by cutdown. Formulas for fluid administration provide only a starting point, and rate of fluid administration must be adjusted according to patient response. At the Children's Hospital of Denver, we have used a formula of 3 cc/kg x% burn for the first 24 hours. Burns of greater than 50 per cent are counted as 50 per cent in the calculation. One-half the calculated volume is given in the first 8 hours and the second half over the next 16 hours. A "composite burn solution" (Table 1) containing 1.25 per cent albumin, approximately two-thirds normal saline, and additional sodium bicarbonate is administered. If weight gain from edema exceeds 10 per cent admission weight, the infusion is slowed and small doses of intravenous diuretics are given.[2]

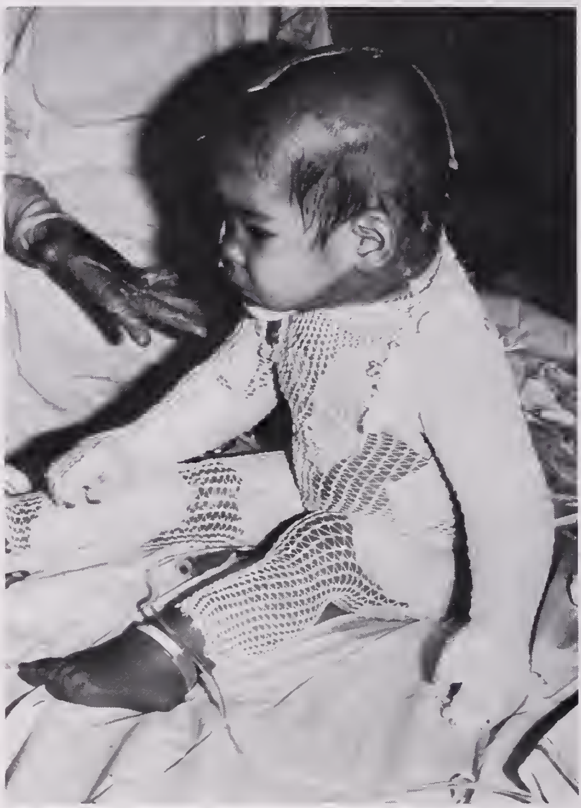

Fig. 1. Dressings containing an antibacterial agent are held in contact with the burn wound by expandible tubular netting. The child has full range of motion in this lightweight dressing, which is changed once daily.

After resuscitation is under way, attention is turned to the burn wound. Cleansing with povidone-iodine soap or dilute sodium hypochlorite is carried out, followed by gentle debridement of blisters and necrotic tissue. Small doses of sedatives may be necessary, but often are not. Circumferential full-thickness burns of limbs may require immediate escharotomy to release a compromised circulation. Occasionally escharotomy is necessary for thoracic burns which constrict respiratory movement.

A nasogastric tube is passed, the stomach contents removed and 30-60 cc of milk instilled hourly. If ileus develops, the tube is placed temporarily to suction until bowel tones reappear. We employ a prophylactic regimen which appears valuable in prevention of Curling's ulcer, consisting of oral administration of milk, 30-60 cc every 1-2 hours around the clock, throughout the post-burn period, until the wound is covered with skin.

The increased caloric requirements of a child with major burns must be met by a high caloric diet, in addition to the milk. Vitamin supplements may be helpful. If the child will not eat, a milk drip via a small indwelling nasogastric feeding tube may be given, with close observation for ileus, to avoid the risk of vomiting and aspiration.

The head of the patient's bed is continuously elevated; this is a favorable position for avoidance of cerebral edema.

Wound Management

Topical antibacterial agents are crucial to reduction of burn wound sepsis. Currently, our choice is silver sulfadiazene spread into a layer of fine mesh gauze, and held in place over the burn wound be a tubular net dressing (Fig. 1). These lightweight dressings are easily applied, and permit considerable mobility of the patient. Silver sulfadiazene does not produce the undesirable side-effects associated with silver nitrate (electrolyte depletion) or mafenide (metabolic acidosis and pain on application).[3]

Daily bathing in a sodium hypochlorite solution (1:60 Chlorox) is carried out, followed by debridement of necrotic tissue from the burn surface. The hypochlorite may diminish bacterial growth in the burned skin, and has a selective in vitro anti-Pseudomonas effect.[4] It also eliminates odor. The daily debridement is effectively accomplished by trained nurses or therapists.

Surveillance for infection requires systematic culture of the burn wound, blood, throat, urine, stool and other sites. Penicillin is given initially for 5-7 days for the prevention of beta-hemolytic streptococcal cellulitis. Systemic antibiotics are not employed thereafter unless there is evidence of sepsis, and they are begun only after adequate cultures of blood, urine and burn wound. The choice of specific antibiotics depend on the patient's current flora. Common sources of infection are: burn wound, pneumonia, urinary or intravenous catheters.

Homograft, usually from cadaver sources, or hetorograft, usually pigskin, provides temporary coverage of a burn wound that is not quite ready for autograft. Advantages of these biologic dressings include (1) a decrease in vapor loss through the burn wound, (2) protection against infection from exogenous sources and (3) dramatic alleviation of pain in the burned area.[5,6]

Tangential excision, a procedure in which the burn eschar is planed off with a dermatome or free-hand knife, has permitted earlier grafting and healing of large burns.[7] Since viable epithelial elements may remain, tangential excision differs from total excision, in which the entire epithelium is removed. The latter procedure is useful for well-demarcated third-degree burns of less than 15 per cent of the body surface, but for larger areas, total excision has in the past carried a significant mortality.[8,9]

Early autografting is extremely advantageous because, once the wound is epithelialized, the risk of burn wound sepsis is nil. The mesh graft, an ingenious technique, permits coverage of larger wounds from limited donor sites. Split thickness graft is passed through a roller device which cuts multiple small slits, allowing the graft to expand as much as three times the original area.[10,11] Epithelium grows from the margins of the lattice-work of graft, covering the interstices within 5-7 days, and closing the wound to exogenous infections.

If many areas are burned, priority in grafting is given to burns of the hands. The earliest possible resumption of hand function for activities of daily living is as important to a child as to an adult.

Rehabilitation

Rehabilitation begins the moment a burned child is admitted. The success of burn care in a child is measured not only in terms of survival but also in the ability of the child to re-enter normal childhood. Prevention of contracture is paramount. In severe burns, skeletal traction may be necessary to prevent assumption of the fetal position, with claw hands and plantar flexion of feet. After third-degree areas are grafted, the traction is removed and the correction maintained by splinting. Active and passive exercises are performed several times daily from the onset, and are omitted only for a two or three day period, immediately following a grafting procedure. A skillful occupational therapist, using appropriate toys and games, can achieve range of motion activity in even the most frightened and reluctant child.

Psychotherapy has become an integral part of burn care. The burned child, like many hospitalized children, feels he is being punished for doing something wrong, which indeed may have been the case at the time of the accident. Parents feel extreme guilt over the burn accident, and they are confronted painfully by the graphic evidence of their apparent neglect. A hospitalized child near death, and facing permanent disfigurement, produces profound emotional and financial strain on the parents. Resulting anxiety may be manifested in such diverse ways as over-solicitousness, wherein a parent insists on staying at the bedside 24 hours a day, or occasionally as hostility of parents to hospital personnel, or to one another. A burn may be unfortunate evidence of the battered child syndrome.[12,13] Although the medical personnel must be sensitive to these important considerations, the handling of psychological and social problems is facilitated by professionals who are an integral part of the "burn team" from the outset.

Grotesque disfigurement due to hypertrophic scar formation may now be diminished by continuous compression of the scar in its proliferative phase, applied by means of elasticised gradient pressure garments custom-tailored specifically for the burned patient.[14,15] These unique little hoods, vests, leotards and suits are producing improved cosmetic results. Injection of the scar with steroids may also be beneficial.

Plastic surgical procedures for release of scar contractures and improved function and cosmesis are usually necessary in the years following a major thermal injury.

The prevention of burns, like the prevention of most accidents and illnesses, has lagged behind their treatment. There is need for epidemiological studies on burns, education of the public and political activism on the part of all physicians who care for children.[16]

Summary

A multidisciplinary team provides optimal care for children with major burns. Successful treatment of a 17-month-old child with a 75 per cent burn required a team strategy for resuscitation, wound care and rehabilitation. •

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Solitary bone cyst of the ilium*

Report of Two Cases and a Review of the Literature

**Kent M. Samuelson, MD, Glenn L. Momberger, MD,
and Sherman S. Coleman, MD, Salt Lake City**

Solitary bone cysts have long been recognized as distinctive and characteristic pathologic lesions. Jaffe and Lichtenstein in 1942 amplified our knowledge of these cysts and clarified some of the issues surrounding them.[8] They pointed out that the cysts grow slowly and are usually discovered as an incidental finding or following a pathologic fracture. They emphasized that the metaphyses of the humerus and femur in the immature skeleton are by far the most common sites for these lesions to occur. Since that time a number of large series of solitary bone cysts have been published.[1,3,5,9-12] The data from these series, including ages of the patients and sites of the lesions, have been combined in Table 1. The figures clearly demonstrate the predilection for the humerus and femur, and the occurrence of the majority in the immature skeleton.

Bone cysts of the ilium are an apparent exception to this pattern. The mean age occurrence at this site is 36, which is twice that of the next older groups consisting of lesions of the calcaneus and radius. Review of the literature adds six more cases in addition to the sixteen in Table 1 for a total of twenty-two cases of solitary bone cysts in the ilium.[1,3,4,6,7,9,11,13] Of this total, the mean age was 35, although the age was not given in three cases. Further, there have been no reported occurrences in the first decade of life and only four occurrences in the second decade.[2-4,9] Because a solitary bone cyst in the ilium is an uncommon lesion and because one in the ilium of an immature skeleton is rare, the following two cases deserve to be reported.

CASE REPORTS

Case 1. A fourteen-year-old female presented with a four week history of pain in the right hip following a fall. Roentgenograms demonstrated a large cystic lesion in the right ilium with a pathologic fracture through the lesion (Fig. 1). The iliac apophyses were present but not closed. A bone survey was negative except for the lesion in the ilium. Hematocrit was 38 and white blood cell count was 6,300 with normal differential. She was taken to surgery where the lesion was curretted and grafted with autogenous iliac bone. Grossly, the cyst contained a large amount of serosanguainous fluid and a fibrous lining. Microscopic examination (Fig. 2) showed the cyst to be lined by a typical connective tissue lining with evidence of peripheral new bone formation and recent hemorrhage, a combination of findings supporting the diagnosis of solitary bone cyst. Roentgenogram one year postoperatively showed repair and filling of the defect by new bone (Fig. 3).

Case 2. A twenty-year-old male was involved in an automobile accident in which he sustained fractures of the left tibia and the pubic rami bilaterally in addition to severe abdominal injuries. An incidental roentgenographic finding was a lytic lesion in the right ilium (Fig. 4). The only history of previous symptoms in this region was at age sixteen when he had pain in the right hip following several hard blows while playing football. Radiographs at that time were normal with no evidence of any lesion in the right ilium. The hip

TABLE 1

Solitary Bone Cysts
Combined data of site and age distribution
of 694 cases in seven reported series.

Location	Number of Cases	Percent of Total	Average Age	Age Range
Humerus	382	55.0	9	1-1/2-42
Femur	193	27.8	13	1-51
Tibia	45	6.5	13	4-36
Calcaneus	23	3.3	18	8-56
Ilium	16	2.3	36	12-72
Fibula	12	1.7	17	5-56
Radius	9	1.3	18	3-38
Miscellaneous	14	2.0	15	1-1/2-45
Total	694			

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*From the Division of Orthopedic Surgery, University of Utah College of Medicine, Salt Lake City, Utah. Dr. Samuelson is Resident; Dr. Momberger is Clinical Instructor; and Dr. Coleman is Professor and Chairman of the Division.

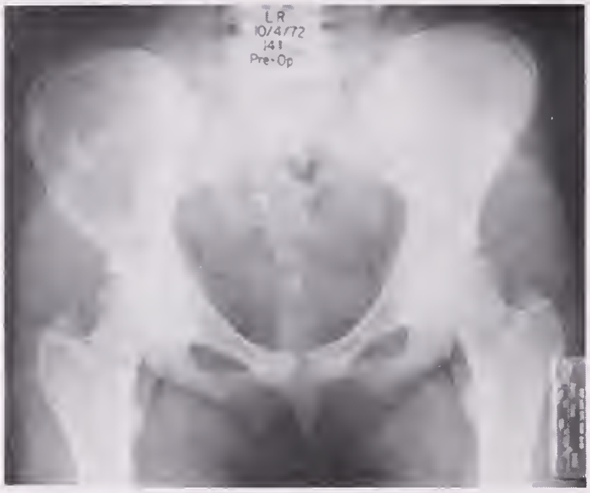

Fig. 1. X-ray film of the pelvis of Case 1 illustrates the large cystic lesion of the right ilium.

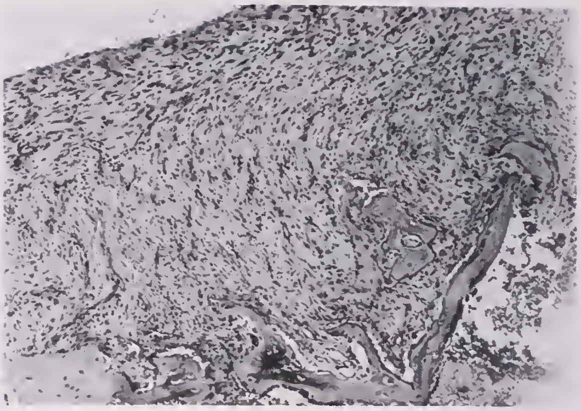

Fig. 2. Photomicrograph of the cyst wall from Case 1 (X 140). Cyst lining containing fibrous tissue and fibroblasts is well demonstrated along with the reactive bone typical of that seen in the periphery of the wall of a bone cyst.

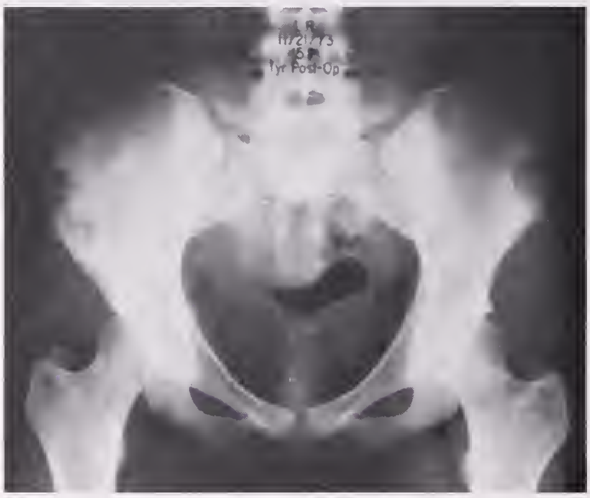

Fig. 3. X-ray film of the pelvis of Case 1 taken one year post-operative showing almost complete replacement of the cyst by bone.

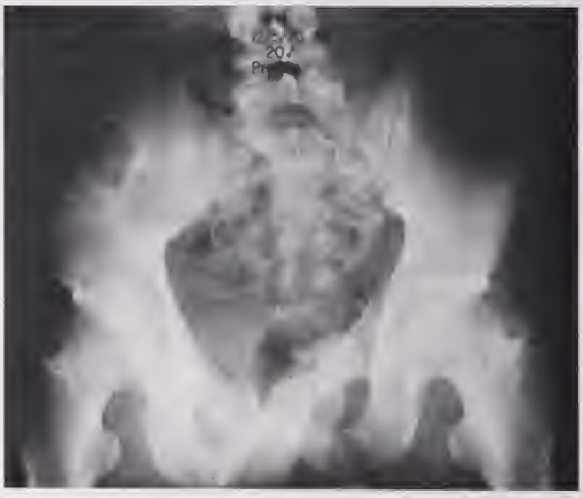

Fig. 4. X-ray film of the pelvis of Case 2 showing multiple pelvic fractures. The radiolucent defect in the right ilium is clearly evident as a well circumscribed cyst-like lesion.

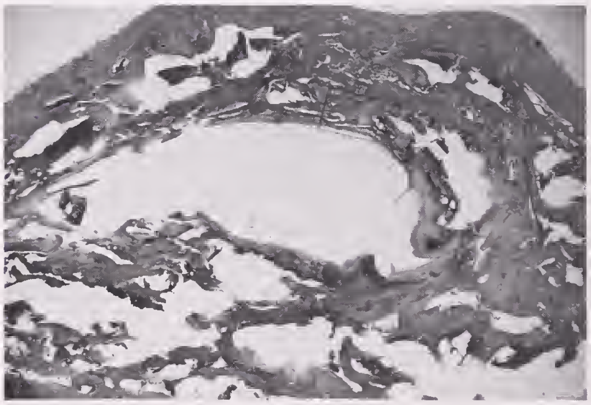

Fig. 5. Low power photomicrograph (X 7) of lesion in Case 2 (Fig. 4) showing well circumscribed cystic cavity with a fibrous lining and peripheral mature and reactive bone.

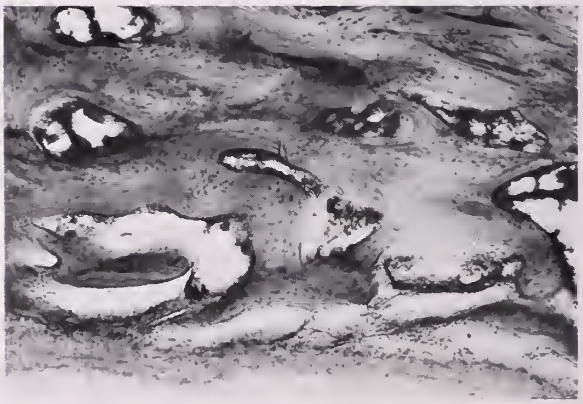

Fig. 6. Photomicrograph at higher magnification (X 60) of area outlined in Fig. 5. This shows the cyst lining and the dense underlying sclerotic bone.

was asymptomatic following that episode until the above accident. Six weeks after the accident he was readmitted to the hospital for diagnosis and treatment of the lesion. Laboratory values at that time were hematocrit 48, white blood cell count 5,600 with a normal differential, chemistry survey normal except for a slightly elevated phosphorus of 5.2 (2.5-4.0) and alkaline phosphatase of 18 (6-15). Because of uncertainty as to the nature of the lesion, an en bloc excision was performed and the defect was packed with homogenous bone. Histologic section of the entire lesion showed a cystic lesion of bone with a thin fibrous lining (Fig. 6). Serial roentgenograms up to four years post-surgery have shown gradual filling of the defect with new bone.

Discussion

The first case report is the fifth recorded instance of a solitary bone cyst encountered in the ilium prior to the third decade. The second case occurred in a twenty-year-old patient who is significantly younger than thirty-five, considered to be the average age for this lesion in the ilium. Of significance clinically is the fact that these cases and this report demonstrate that solitary bone cysts occur in the ilium over a wide age distribution and this diagnosis must be considered in the differential of a lytic lesion of the ilium. •

ACKNOWLEDGEMENT

The authors express appreciation to Dr. Gilbert G. Tobler for allowing inclusion of his patient in this report.

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Emergency Treatment of Drug Overdose*

George B. Guarino, MD, and
Nampalli K. Vijay, MD, Denver

ALTHOUGH ATTEMPTED SUICIDE basically represents a psychiatric problem, the patient who makes such an attempt is often seen by a general practitioner or internist. With the development of emergency room services, more of these problems will be received for initial treatment in these locations, and the method of managing such clinical situations becomes an important concern of these disciplines. Furthermore, since an increased number of cases will be seen in the emergency room,[1] and since the most common suicide attempt is ingestion of an overdose of a sedative or hypnotic medication,[2] the approach to managing the state of intoxication with such drugs merits thorough review.[1]

Our experience of the past two years, forty-three patients, is summarized in Table 1. It is the purpose of this brief presentation to summarize a ready reference with key features that the physician must know when presented with the acute condition of overdosage.

TABLE 1

DRUG OVERDOSE TREATMENT*

Number of patients treated	43
Number of survivors	40
Number of deaths	3

* *Twenty-nine patients were in actual coma, 11 were aroused with difficulty, and 3 were easily aroused. One of the patients who expired was aroused easily, but rapidly became comatose from overdose of Darvon. In the usual instance, the actual drug taken was non-recoverable.*

Management

When first observed, patients are usually semi-comatose or comatose. As a general approach, the following steps should be taken:

(1) Perform gastric lavage with tap water or saline.
(2) Protection against aspiration.
(3) Establish and insure adequate airway.
(4) Institute a vigorous and regular monitoring of vital signs, with particular focus on maintaining an adequate blood pressure.
(5) Place the patient in a protected and supervised setting, preferably the hospital, for supportive care.[3]
(6) Draw blood levels and obtain urine samples.

Having accomplished these initial steps, the next immediate question is whether a specific antidote (or stimulant) may be used or whether some type of clearance of the agent from the patient's tissues can be effected. Experience during the past several decades has indicated that stimulants such as picrotoxin, amphetamine, or caffeine appear to be of little help in modifying the course of patients with an overdose of sedative or hypnotic medication.[4] The major problem is whether the drug can be rapidly cleared from the tissues of the body, and it is with this purpose in mind that the technics of dialysis and forced diuresis (200-500 cc/hour)[1,5] have now become important procedures in the treatment of these patients. However, conservative, supportive care must not be underestimated if dialysis is not available.[6]

There are many proponents of employing dialysis or induced diuresis in order to more rapidly clear the drug or drugs.[6-10] In the preparation of ready reference table (Table 2), a thorough search of the literature and a series of

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TABLE 2

DRUG OVERDOSE TREATMENT FOR COMMONLY USED DRUGS*

SEDATIVES AND TRANQUILIZERS	Estimated Fatal Dose	Other Clinical Findings	Treatment (Dialysis and/or Osmotic Diuresis)
1. Glutethimide (Doriden)	10-15 gm.	Apnea, varying levels of consciousness, cerebral and pulmonary edema, pancytopenia & leukopenia	Diuresis ineffective, Megimide antagonistic, dialysis moderately effective
2. Diphenylhydantoin (Dilantin)	2-4 mg.	Respiratory distress, swelling, coma, liver and kidney injury, agranulocytosis	Dialysis most effective, bound to plasma proteins
3. Diazepam (Valium)	5-10 gm.	Apnea and circulatory distress but often causes neither	Dialysis minimally effective
4. Primidone (Mysoline)	5-7 gm.	Respiratory distress, swelling, coma, liver and kidney injury, agranulocytosis	Good
5. Meprobamate (Miltown) (Equanil)	15-40 gm.	Fever, chills, periorbital edema, aplastic anemia, purpura, respiratory & circulatory failure	Forced diuresis and dialysis effective
6. Ethchlorvynol (Placidyl)	10-25 gm. (5 mg% blood level)	Cerebral dysfunction, circulatory and respiratory failure	Poor
7. Chlordiazepoxide (Librium)	275 mg.-1 gm. (0.-0.5 mg% blood level)	Rage reaction, agranulocytosis convulsions	Forced diuresis or dialysis minimally effective
8. Chloral hydrate	2-5 gm.	Rapid circulatory failure, liver and kidney injury	Forced diuresis or dialysis minimally effective
9. Flurazepam hydrochloride (Dalmane)	5-15 gm.	C.N.S. symptoms, G.I., G.U. complaints	Forced diuresis or dialysis minimally effective
10. Phenothiazines (Thorazine) (Sparine) (Vistaril)	75 mg.	Agranulocytosis, circulatory and liver failure, convulsions, paralysis	Forced diuresis or dialysis minimally effective
11. Heroin	0.2-0.3 gm.	Acidosis, respiratory and cardiac failure, convulsions	Dialysis effective, forced diuresis minimally effective
12. Meperidine hydrochloride (Demerol)	1-2 gm.	Respiratory, circulatory, renal failure, convulsions	Dialysis minimally effective, forced diuresis ineffective
13. Morphine	0.2-0.3 gm.	Respiratory depression, circulatory failure, convulsions	Dialysis moderately effective, diuresis minimally effective
14. Dilaudid	0.1-0.2 gm.	Respiratory depression, circulatory failure, convulsions	Dialysis moderately effective, diuresis minimally effective
15. Phenobarbital	10-20 gm.	Respiratory and cardiac failure, renal failure	Forced alkaline diuresis ineffective, dialysis effective
ANALGESICS			
1. Acetylsalicylic acid (Aspirin)	5-50 gm. (50-150 mg% blood level)	Respiratory stimulant and has imbalance ketosis disease, protemia, acidosis and hypokalemia, clotting abnormalities	Forced diuresis with alkalinization of urine, dialysis effective
2. Propoxyphene hydrochloride (Darvon)	1-2 gm.	Convulsions, respiratory depression, pulmonary edema, early low blood levels	Forced diuresis and dialysis in combination minimally effective
HALIDES			
1. Bromide Bromural Carbromal Bromoform	10-20 gm. (300 mg.% blood level)	Low chlorides	Rapid - replace chloride
ALCOHOLS			
1. Ethanol	500-1000mg.% blood levels	Coma, acidosis, blindness, renal and respiratory failure	Forced diuresis and dialysis effective
2. Ethyl	300 mg.% blood levels	Respiratory and cardiac failure, seizures	Dialysis effective, forced diuresis minimally effective
3. Methanol	250 mg.% blood levels	Central nervous system depressant, acidosis, renal failure, blindness	Dialysis effective
4. Ethylene glycol	Unknown	Ataxia, tachycardia, pulmonary edema, kidney failure	Dialysis effective
5. Isopropyl	300-500mg.%	Circulatory collapse, apnea, cherry red skin and mucous membranes	Dialysis effective, diuresis minimally effective
METALS			
1. Bal-Mercury complex	In excess of 1000 micrograms	Renal and liver failure	Poor
2. Arsenic	Unknown	Hemolysis, liver and renal failure, convulsions	Hemodialysis effective

** A composite of standard textbook references and drugs found in the review by Schreiner and Teehan in 1972*[1] personal communications were conducted in order to collect the documented instances of the efficacy or lack of efficacy of these technics for the various drugs that are now available. Since the number of sedative and hypnotic drugs has increased during the past several years, there is an appreciable lag between clinical experience with these agents and the description of this experience in the medical literature. Accordingly, not all presently-employed drugs may be listed. The list is up-to-date as of May 1975.

Drugs have been listed and categorized according to the everyday parlance of the practicing physician. The amount of medication which has been considered represents the minimal total dosage which has been reported to have actually resulted in death. No attempt was made to match weight, age, sex, existence of other diseases or other factors which might significantly determine whether a given dose proves to be fatal. In most instances the patients were otherwise well, weight was around 150 pounds, and ages generally fell in the 25-45 year range.

The column labeled "Other clinical findings" lists some of the other toxic manifestations that have been reported. No such notations are made for the barbiturates since the characterization of the toxicity of these agents is well reviewed in all texts of pharmacology and toxicology.

In regard to the estimate as to whether dialysis and/or osmotic diuresis is effective in enhancing removal of the drug, three types of responses have been classified: rapid (clearance within 24-48 hours), slow (48-72 hours), and ineffective (96 hours or longer).

Summary

Review of the clinical experience and methods used in our hospital for emergency treatment of drug overdosage. A guide to the applicability of dialysis/diuresis therapy in such patients is provided. Emphasis for supportive or conservative treatment should not be underestimated when dialysis is not immediately available. •

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The authors wish to thank Doctors Richard E. Holman and Wagner J. Schorr, Denver, for their valuable professional assistance and review of this manuscript.

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Dr. Watson of Baker Street

E. D. Morton, MD, Ogden, Utah

ALMOST A CENTURY has passed since Dr. John Watson met Sherlock Holmes in the chemical laboratory of St. Bartholomew's Hospital in London. This meeting marked the beginning of their adventures together, yet the popularity of the stories — narrated primarily by Dr. Watson — has never waned. Watson, writing about their first case together in *A Study In Scarlet,* carefully recorded the circumstances of the meeting at "Bart's". This encounter, the unspectacular beginning of their association, is suitably commemorated by a bronze plaque at the site.

Although Holmes criticized Watson's literary style, he eventually conceded that Watson was "my Boswell". Watson's narrative style was particularly effective for he modestly told little about himself, preferring to write about the exploits of his friend. His reticence has left us with little biographical material, but scattered through the various accounts of Holmes' cases enough information can be found to piece together a passable character study.

Of his early life little is known. He had an older brother who was an alcoholic. He attended a "well-known public school". He took his medical degree at the University of London in 1878. Three years military service in Afghanistan left him in ill health and with wounds — inflicted by "a Jezail bullet" — which were a long time healing. In 1881, when he was approximately thirty years old, he returned to England.

> "I had neither kith nor kin in England, and was therefore free as air — or as free as an income of eleven shillings and sixpence a day will permit a man to be. Under such circumstances I naturally gravitated to London, that great cesspool into which all the loungers and idlers of the Empire are irresistably drained" *(A Study In Scarlet).*

At the Criterion Bar he met "young Stamford, who had been a dresser under me at Bart's". Watson mentioned that he was looking for a room but that his income was limited. Stamford replied that he had heard a fellow at the hospital bemoaning the fact that he had found some rooms and could not get anyone to share the rooms and the rent. Hence the meeting with Holmes. At the end of the meeting Holmes asked Watson to "call for me tomorrow and we'll go and settle everything".

It appeared that Holmes quickly recognized in Watson a complementary personality, but Watson initially found his companion a rather strange fellow. For several days Watson wondered about Holmes' line of work, but found himself unable to ask a direct question. Not until the detective almost accidentally demonstrated his amazing powers of observation and deduction, and confided that he was a "consulting detective", did Watson unbend. Thereafter his admiration and devotion never waned.

Although somewhat conservative in his outlook, Watson understood and tolerated Holmes' eccentricities. It may have been that Watson indeed had some "natural Bohemianism of disposition" that he once mentioned, or his medical and military experiences might have prepared him for his association with Holmes. Even Holmes's addiction to cocaine and morphine did not alarm him. Happily he was able to assist the detective in overcoming the habit, no small accomplishment considering the difficulties Osler had with Halstead a few years later.

The relationship between the two friends could best be explained by Watson in the statement he prefixed to the adventure of *The Creeping Man*:

> "The relations between us were peculiar. He was a man of habits, narrow and concentrated habits, and I had become one of them. As an institution I was like the violin, the shag tobacco, the old black pipe, the index books, and others perhaps less excusable. When it was a case of active work and a comrade was needed upon whose nerve he could place some reliance, my role was obvious. But apart from this I had uses. I was a whetstone for his mind; I stimulated him. He liked to think aloud in my presence. His remarks could hardly be said to be made to me — many of them would have been as appropriately addressed to his bedstead — but none the less, having formed the habit, it had become in some way helpful that I should register and interject. If I irritated him by a certain methodical slowness in my mentality, that

> irritation served only to make his own flame-like intuitions and impressions flash up the more vividly and swiftly. Such was my humble role in our alliance."

Despite his dog-like devotion to Holmes, Watson managed to have a life of his own. He was twice married. He had a practice in the Paddington district of London. Although not wealthy, he was able to take leave of his practice (and each of his wives) at a moment's notice whenever Holmes needed him. He was competent in his field. He saved the life of Jephro Rucastle in *The Adventure of the Copper Beeches,* and skillfully attended Victor Hatherley's injury in *The Adventure of the Engineer's Thumb.* He knew his way about the hospitals of London. He always read the *British Medical Journal,* and was familiar with other medical writing of his day, as he demonstrated in *The Resident Patient.* All told, he apparently had the best of two worlds, although there was no doubt where his primary interests lay. But fair allowance must be made for the state of his health — it is doubtful that he could have withstood the rigors of a full-time practice. On the other hand, his association with Holmes frequently required exhausting journeys, occasional dangerous encounters with hardened criminals, and at least two frightening experiences with vicious dogs. And in *The Hound of the Baskervilles* he pursued an escaped convict over the rugged moors with no difficulty. No mention was made of his war wounds at this time. On the contrary, he gave the impression that his health was excellent.

Had Watson engaged in full-time practice, however, the world would have been poorer for it. Holmes could never have found a better biographer or more devoted friend. No one else could have been a better foil for the many-sided sleuth, and few would have tolerated his eccentricities. Watson's medical training enabled him not to be shocked at some of the gory aspects of Holmes' cases, yet he was always properly surprised at a revelation of some hidden detail. He consistently understated his part in the various adventures, causing Holmes once to remark:

> "Watson, you excel yourself. I am bound to say that in all the accounts which you have been so good to give of my own small accomplishments, you have habitually underrated your own abilities . ."

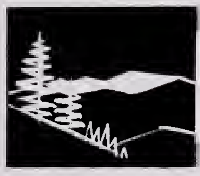
But understatement can be quite effective. While he omitted the details of his participation in Holmes's cases, he established the name of his friend as a household word throughout the entire literate world.

The character of John Watson was apparently a composite created by Conan Doyle. His name was originally conceived as "Ormond Sacker" but Doyle felt that it smacked of dandyism. Casting about for an appropriate name he borrowed the surname of a friend of Portsmouth, Dr. James Watson. Watson's physical appearance was drawn from a Major Wood, another Portsmouth friend who served as Doyle's secretary for many years. One suspects that some of Watson's mannerisms and personality were drawn from his creator, for Doyle himself was a physician before he turned to writing.

The character of Holmes, of course, was based on that of another physician, Dr. Joseph Bell of Edinburgh, and doctors were often encountered in the various adventures. Dr. Joseph Mortimer *(The Hound of the Baskervilles)*, Dr. Percy Trevelyn *(The Resident Patient),* and Dr. Grimesby Roylant *(The Adventure of the Speckled Band)* are the best known. Not all of them were notable examples of the medical profession, and it is probable that they were modeled after medical acquaintances of Doyle.

But the character of Watson is as real as that of Holmes. We see him as he falls in love, as he practices his profession, as he dutifully accompanies Holmes to some obscure destination, and as he grieves after Holmes' supposed death in the encounter with Moriarity. He never ceases to marvel over the detective's great gifts. We see him blush at Holmes' remark: "The fair sex is your department, Watson", and we see a stern, resolute figure, carefully checking his service revolver, when his friend says: "It is in the hour of action when I turn to you for aid". An anonymous narrator gives us the last glimpse we have of him at about age sixty, "a heavily built elderly man with a gray moustache . . . sitting at the wheel, like one who resigns himself to a long vigil *(His Last Bow)*".

Watson became famous only because of his association with Holmes. Perhaps Holmes would have gained his fame without Watson, but it is doubtful, for something is lacking in the stories that are not narrated by Watson. In being Holmes's Boswell, Watson gained his own share of fame, and for a physician who never wrote a paper, who practiced in obscurity in the shadow of a narcotic addict—and who never existed—he has certainly endured. •



COLORADO

McIntosh To Receive Johnson Award

Rawle McIntosh, 37, MD, associate professor of pediatrics and medicine, associate professor of clinical immunology and head of pediatric nephrology at the University of Colorado Medical Center, Denver, has been selected by the American Academy of Pediatrics (AAP) to receive one of two $3,000 E. Mead Johnson Awards in pediatrics.

West Indian-born Doctor McIntosh will receive his award for his original and significant contributions in the field of immunologic mechanisms in renal disease. He was among the first investigators to appreciate the significance of cryoglobulins in relation to the pathogenesis and prognosis of renal disease.

Doctor McIntosh's work in pathology and immunopathology, including the finding of several antigenic causes of glomerulonephritis has added to our understanding of pathogenic mechanisms, both in experimental animals and in man. The antigenic relations he has demonstrated between basement membranes of various organs, including the placenta, may hold promise for the understanding of developmental defects in children.

He received his M.D. degree from New York Medical College in 1963. He took his pediatric residency at the University of California, San Francisco and at Stanford University. He was a postdoctoral Fellow at the University of California, Los Angeles, and a research associate at La Rabida-University of Chicago Institute.

Kern Elected Gastroenterological President

Fred Kern, Jr., MD, head, University of Colorado Division of Gastroenterology, has been elected president of the American Gastroenterological Association. Doctor Kern, who received his M.D. from the Columbia University College of Physicians and Surgeons, New York, is the author or co-author of more than 90 articles on such topics, as constipation, diarrhea, comprehensive medical care, bile salt metabolism and malabsorption, and ulcerative colitis.

Doctor Kern is a member of the scientific advisory board of the National Foundation for Ileitis and Colitis. He also belongs to the International Association for the Study of the Liver, American Institute of Nutrition, American Federation for Clinical Research, American Clinical and Climatological Society, American Association for the Study of Liver Disease, Alpha Omega Alpha and other professional organizations.

Doctor Kern came to the CU School of Medicine in 1952 as an assistant professor of preventive medicine and public health. He was appointed head of the gastroenterology division in 1959 and professor of medicine in 1965.

Kresge Grant To National Jewish Center

The Kresge Foundation of Troy, Michigan has approved a grant of $125,000 for the National Jewish Hospital and Research Center to be used for a gymnasium in the new Therapy and Learning Center, soon to be constructed, at an estimated cost of $600,000. The contribution by The Kresge Foundation advances the realization of a need for a new structure that will house therapy and learning activities, which will include the gymnasium.

The Kresge grant is conditioned upon the raising of the $600,000 required to complete the Therapy and Learning Center.

It is anticipated that groundbreaking for the new N.J.H. Therapy and Learning Center will take place in about 90 days.

MEDICAL SCHOOL NOTES

Ott Elected President, Clinical Toxicology Academy

John Ott, MD, associate professor of pediatrics, University of Colorado School of Medicine, has been elected president of the American Academy of Clinical Toxicology. After receiving his M.D. in 1963 from the University of Pittsburgh Medical School, Doctor Ott did his internship at the Children's Hospital of Pittsburgh and his pediatric residency at the CU Medical Center. Since 1971, he has been the co-director of the Child Health Associate Program at UCMC. Doctor Ott is the former director of the Physician's Poison Consultation Service and former assistant director of the Birth Defects Center at UCMC.

Doctor Ott is a member of several professional organizations including the American Association of Poison Control Centers, National Association for Retarded Children, Health Education Media Association, Association of Schools of Allied Health Professions and the Western Society for Pediatric Research.

Vernadakis Receives Epilepsy Grant

Antonia Vernadakis, MD, associate professor, University of Colorado Departments of Psychiatry and Pharmacology, has received an $11,045 research grant from the National Epilepsy Foundation of America to study the effects of Dilantin, a major anticonvulsant, on the growth of developing brain tissue. Cultures for the study will be obtained from chick embryos. She will study the variety of poisonous effects of different cellular types of brain tissue.

The grant was awarded by Luther Glass, a member of the board of directors of the Colorado Epilepsy Association and the regional delegate to the national foundation.

Sauerbier Named Acting Chairman, Biophysics and Genetics

Walter Sauerbier, MD, has been appointed the acting chairman of the University of Colorado Department of Biophysics and Genetics. Born in Butzbach, West Germany, Doctor Sauerbier did graduate work in biophysics at the *Max Planck Institut fuer Biophysik,* Frankfurt-Main, West Germany. From 1959-61 he was an official assistant at the *Institut fuer Genetik, Universitaet Koeln,* West Germany.

Doctor Sauerbier, 43, was a visiting investigator at the Institute of Molecular Biology, University of Oregon, Eugene, from 1961-62 and again from 1965-66. He is the author or co-author of more than 35 articles.

He came to the CU Medical Center in 1966 as an assistant professor of biophysics and genetics.

March of Dimes Grant

David Wenger, MD, assistant professor of pediatrics and neurology, University of Colorado Medical Center, has received a $56,000 March of Dimes research grant for two years to study the variations in human enzyme chemistry which lead to Gaucher disease, an inherited metabolic disorder. This disease takes several forms, ranging in severity from a mildly enlarged spleen and tendency to bone fractures to an early onset kind which attacks infants during their first few months of life and usually kills them before they reach two years of age.

All types of Gaucher disease involve the body's inability to produce an active form of an enzyme called beta-glucosidase. Normally, this enzyme breaks down a lipid sugar complex, glucosyl ceramide. However, in Gaucher disease, the sugar complex accumulates in many body tissues and sooner or later interferes with their functions.

It has been difficult, until recently, to isolate glucosyl ceramide from tissues or to synthesize it for experiments. Using new technics, Doctor Wenger hopes to make clear how it is broken down by beta-glucosidase, and to determine whether more than one form of the enzyme is at work. He believes that the differences in symptoms among the types of Gaucher disease may reflect two or more chemically similar, but functionally different, forms of the enzyme.

THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Recent Acquisitions

American Men and Women of Science, Medical Sciences: Jacques Cattell Press, ed. N.Y., Bowker, 1975. 1269 p. $42.50.

Canadian Hospital Directory, 1975: Kaye Finch, ed. Toronto, Canadian Hospital Association, 1975. 348 p. $18.00.

Canadian Medical Directory, 1975: Don Mills, Ontario, Seccombe House, 1975. 268 p. $15.00.

The CIBA Foundation: An Analytic History 1949-1974: F. Peter Woodford. Amsterdam, Elsevier, 1974. 212 p. Gift.

Energy Transformation in Biological Systems: Amsterdam, Elsevier, 1975. 416 p. (Ciba Foundation Symposium 31) Gift.

Gout: John H. Talbott. 2nd ed. N.Y., Grune and Stratton, 1964. 261 p. Gift.

An Historical Account of Pharmacology to the 20th Century: Chauncey D. Leake. Springfield, Ill., Thomas, 1975. 210 p. Review copy. $12.50.

Laughter and the Sense of Humor: Edmund Bergler. N.Y., Intercontinental Medical Book Corporation, 1956. 297 p. Gift.

Mental Evaluation of the Disability Claimant: Frank O. Volle. Springfield, Ill. Thomas, 1975. 121 p. Gift.

Mortality and Morbidity in the United States: Carl L. Erhardt and Joyce E. Berlin, eds. Cambridge, Harvard Univ. Press, 1974. 289 p. $10.00.

The New Management of Stable Adult Diabetes: Charles Weller. Springfield, Ill., Thomas, 1969. 162 p. Gift.

Peripheral Arterial Disease: Wiley F. Barker. 2nd ed. Philadelphia, Saunders, 1975. 503 p. (Major problems in clinical surgery, v. 4). $15.75.

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The Children's Hospital

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James Kennedy Todd, MD, Speaker

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October 24, 1975

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Lomotil is contraindicated in children less than 2 years old.

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Each tablet and each 5 ml. of liquid contain: diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming), atropine sulfate 0.025 mg

holds the line.

IMPORTANT INFORMATION: *This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration

The idea of a so-called patien package insert has been around fo a long time. Many physicians alrea use written instruction sheets to provide patients with information about the drugs they are taking. Ar some physicians give verbal instru tions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit wit glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official packag insert for patients is a good one. Perhaps we should really think of this kind of information simply as a extension of drug labeling.

The benefits of patient involvement

Many physicians may not rea ize how frequently a patient obtain his drug information from Aunt Tillie or the next door neighbor. An this information is almost always bad or irrelevant to the case at han Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impresse by the principle that the best way t get someone to do something is to involve him in the process. So the

Dr. James H. Sammons
Executive Vice President
of the American
Medical Association

I think there are advantages a well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complication or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a packag insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

ain purpose of drug information r the patient is to get his coopera- on in following a drug regimen.

eparation and distribution of atient drug information

We would hope to amass infor- ation from physicians, medical ocieties, the pharmaceutical indus- y and centers of medical learning. ne ultimate responsibility for uni- rm labeling must, however, rest ith the Food and Drug Administra- on. There is nothing wrong with is agency saying, "this informa- on is generally agreed upon and erefore it should be used," as long s our process for getting the infor- ation is sound.

Distribution of the information a problem. In great measure it ould depend on the medication in uestion. For example, in the case f an injectable long-acting proges- erone, we would think it mandatory issue two separate leaflets—a hort one for the patient to read be- ore getting the first shot and a long ne to take home in order to make a ecision about continuing therapy. n this case, the information might e put directly on the package and ot removable at all. But for a medi- ation like an antihistamine this nformation might be issued sepa- ately, thus giving the physician the ption of distribution. This could reserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

---

nly the doctor can remove that fear y 20 or 30 minutes of conversation.

I'm not suggesting that we ithhold any information from the atient because, first of all, it would e totally dishonest and secondly, it ould defeat the very purpose of the nsert. I do think that a patient on the irth control pill should know about he incidence of phlebothrombosis.

If you're going to tell a patient he incidence of serious adverse re- ctions, then you have to tell him hat a concerned medical decision vas made to use a particular medi- cation in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, be- cause of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* WARNING
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

* **Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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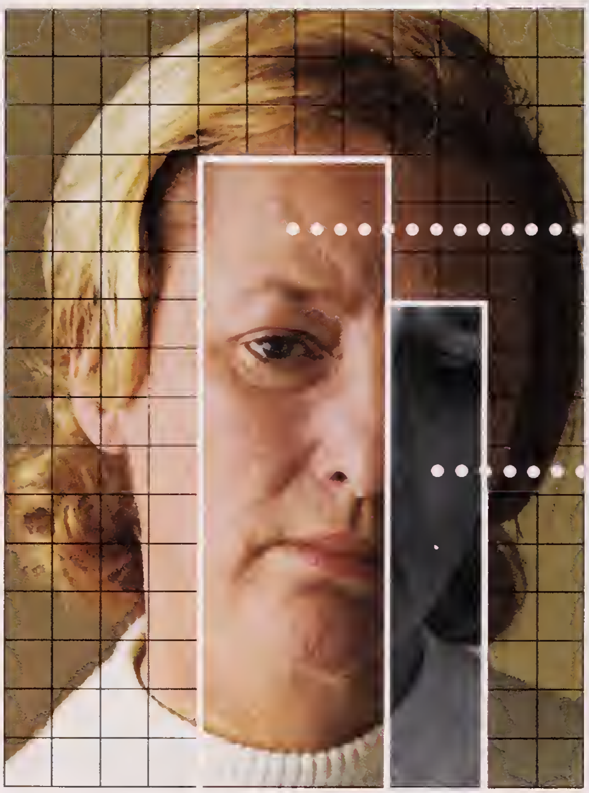
Predominant psychoneurotic anxiety
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Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequenc and/or severity of grand mal seizures ma require increased dosage of standard ant convulsant medication; abrupt withdrawa may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and mus cle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major symptoms, she is a psychoneurotic patient with severe anxiety. But according to the description she gives of her feelings, part of the problem may sound like depression. This is because her problem, although primarily one of excessive anxiety, is often accompanied by depressive symptomatology. Valium (diazepam) can provide relief for both—as the excessive anxiety is relieved, the depressive symptoms associated with it are also often relieved.

There are other advantages in using Valium for the management of psychoneurotic anxiety with secondary depressive symptoms: the psychotherapeutic effect of Valium is pronounced and rapid. This means that improvement is usually apparent in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium®
(diazepam)

2-mg, 5-mg, 10-mg tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

surveillance because of their predisposition to habituation and dependence. In pregnancy, lactation or women of childbearing age, weigh potential benefit against possible hazard.

Precautions: If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

ROCHE

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Nutley, New Jersey 07110

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Letters TO THE EDITOR

To the Editor:

In Doctor Smith's editorial on malpractice, he suggests that we physicians are scapegoats. I'd like to try an alternative analysis.

The medical system that we work under has evolved under the dominant influence of physicians, with minor modifications (Medicare, Medicaid) forced upon the profession at times of crisis. The basic system (fee for service, practitioners licensed by the state) places a premium on the freedom of the practitioner to do whatever is deemed appropriate. In this system, the patients are at the mercy of the practitioner since they cannot treat themselves (prescription drug laws forbid it) and the cost of multiple consultations is prohibitive. The only quality control in this system is the ability of the patient to sue for damages if harm is done by the practitioner. This system offers great benefit to physicians, but there are no advantages to the patient that wouldn't also be available under alternative systems.

Organized medicine, encouraged by corporations trying to maximize profit (insurance companies, manufacturers of medicines and devices), fosters a belief in the general public that we physicians possess unlimited healing powers, and that we regularly perform miracles in office and hospital. An uncritical press disseminates this line throughout the country to the extreme that new cures for cancer are regularly reported. Further, many physicians, possibly because they feel threatened or possibly because they believe the public to be incredibly stupid, are unwilling to discuss indications, complications, or side effects of procedures or medications (the mechanic takes care of my car, I'll take care of your body, dearie).

All of this might be tolerable if we had evidence that Americans were extraordinarily healthy. Instead we have consistently shown that we are unable to keep up with poorer countries in our ability to save our children and elderly from premature death. We tolerate incompetence among our peers, and we accept calmly unnecessary surgery and the common use of unnecessarily dangerous or inappropriate drugs. We accept in our journals advertising that is blatantly misleading and we let these ads influence our prescribing. We fight any effort to limit out prerogatives, and yet we are unable to police ourselves.

Most medical practitioners are able, conscientious people. My criticism is not aimed at individuals, but to the system we work in. The increase in malpractice awards primarily is a reflection of the shortcomings of that system. Instead of crying for relief from malpractice judgements, we should listen to people crying for relief from malpractice, and help establish a system that is equitable to the patient as well as the practitioner.

The mid twentieth century may be the zenith of medicine, but if it declines from here I think that we only need look toward ourselves for the cause.

Sincerely,
Matt Kelly, MD
Santa Fe, New Mexico

Reader commentaries are always enlivening. The Journal welcomes your thoughts, criticisms, and observations.

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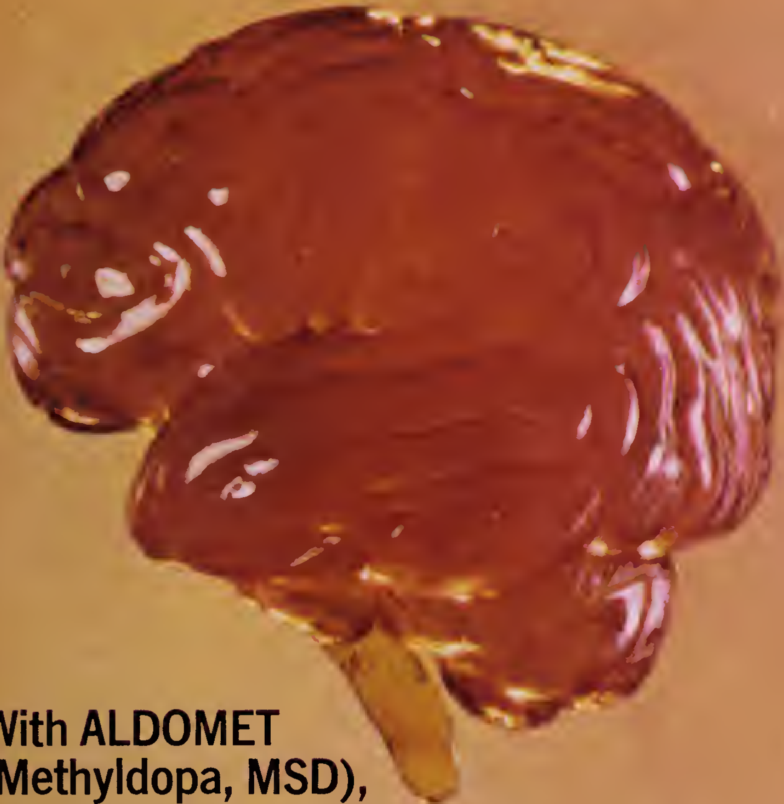

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Warnings: It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

Use in Pregnancy: Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

Precautions: Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

Adverse Reactions: *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

Cardiovascular: Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

Gastrointestinal: Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

Hepatic: Abnormal liver function tests, jaundice, liver disorders.

Hematologic: Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia.

Allergic: Drug-related fever, myocarditis.

Other: Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

Note: Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

How Supplied: Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

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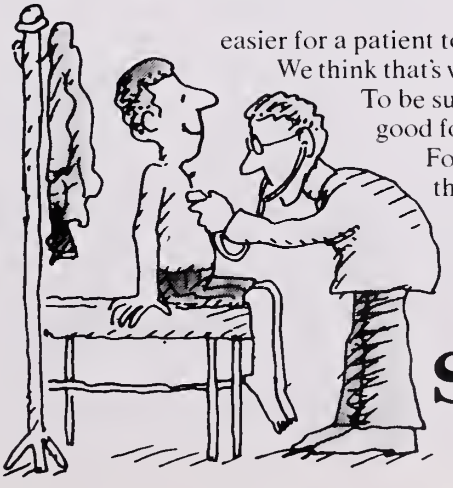

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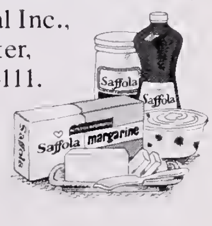

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***Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. **Accordingly, check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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Nevada State Medical Association

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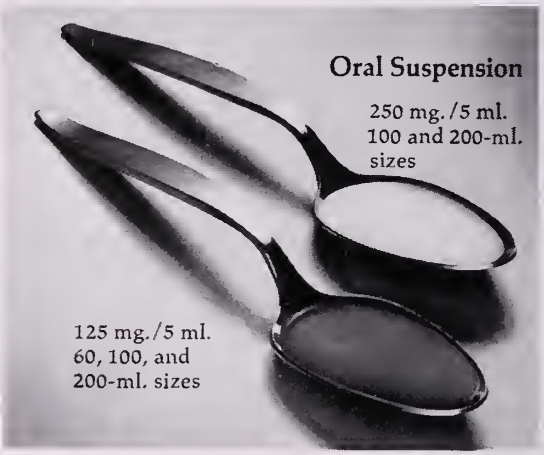

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Reflections of Infant Mortality and a Nation's Health

It has become fashionable to use mortality rates and life expectancy estimates as indications of the health care of a nation. Of these, the infant mortality rate (IMR) has received the most publicity. We are constantly reminded in newspapers, magazines, and releases from government agencies that the United States ranks somewhere between tenth and 28th on international IMR lists, depending on the year of the listing and the number of tabulated countries. An example is the White Paper of 1971: "The United States is not performing as well as other advanced nations. Our ranking as 13th in infant mortality is the key indicator of poor performance. Even if the statistical variations were straightened out, there would be little rejoicing. For the belief is that the United States with its great abundance should have the lowest infant death rate, and the expectations are that it can achieve this rank."[1]

Rarely mentioned is the dramatic decline in the IMR in the USA. Between 1945 and 1974 it dropped from 38 to 17.6 (provisional) per 1,000 new births per year. Usually mentioned is Sweden, the country with the lowest or second lowest IMR, a rate attributed to its health care and social welfare system. Our higher IMR has been blamed on the American Medical Association because it "has selfishly discouraged medical school enrollments in order to keep the number of doctors down and their incomes up." Accordingly, the way to improve our health indicators is to turn out more doctors, as does the Soviet Union; with only seventeen per cent more population it has 350 per cent more physicians, so many that it is able to export 2,000 to help sick people in emergent countries.[2] Unmentioned is the IMR of the USSR, always much higher than ours.

Not surprisingly, indignant editorials and letters have brightened the dull pages of medical journals, contending that "paranoia" is rampant, as well as "nationalistic defensive propaganda writing", that our position on the list is "a disgrace," "impossible," "incredible," "totally unacceptable," "shame denoting," the result of "statistical manipulation," "incomplete reporting," "gimmicks," or "erroneous conclusions" or that "money cannot buy health," because the important causes of death and disease in our country are cancer, heart disease, vascular lesions, hunger, war, automobile accidents, obesity, drug overdose, pollution, lack of exercise, and smoking—many of these stemming from the affluence of our society. We also read that the great reduction in mortality in this century has been achieved only because we have learned to control infectious disease. This statement is sometimes followed by the prediction that future significant gains can be achieved only through the control of chronic disorders and "diseases" of society.

In the past, when lay friends asked about the health indices, the AMA, or Sweden's national health plan, I would uncomfortably suggest that health statistics were often misused and could prove anything one wished to prove, quoting old saws like the average man and his dog have three legs each, or the chances of dying in a hospital are greater than of dying at home.[3] Then, defensively, I would point out that in the last decade the AMA had vigorously dunned its members for contributions to prevent medical schools from foundering on the shoals of inflation and expansion. I would tell of the AMA's support of the historic Flexner Report which led to the elimination of inadequate, commercialized medical schools, and I would expand upon the AMA's educational councils and committees which labor to establish and maintain high standards of education at all levels. About

Sweden I would say that I knew more about its smorgasbord than its health care system.

That these statements satisfied no one prompted a study of the mysterious world of vital statistics.

Data Shortcomings

Data for the indices are collected at the National Center for Health Statistics (USPHS) and the Statistical Office of the United Nations. Countries placed on international lists are required to report more than ninety per cent of their vital events (births, deaths), but the nations themselves determine the completeness of the submitted data. Admittedly, data collection is imperfect, with errors of coverage, content, sampling presentation and interpretation. Definitions differ. The time base for registration and reporting of events is variable. Not only are actual figures used, but also, of necessity, provisional or limited figures. Furthermore, data of a certain year are often compared with data of a different year, but if the years are not too out of joint such comparisons are said to be acceptable.[3-5]

A few examples. What is a viable infant? "Any sign of life" regardless of gestational age such as respiratory effort, pulse, violent movement? Until 1960, the only criterion in Sweden was breathing. In the USA, each state has its own criteria for reporting births and deaths. In the United Kingdom births at less than 28 weeks are considered still births; in Finland, infants less than 800 grams are not included in still born statistics. In England and Wales events are tabulated by year of occurrence, in Northern Ireland and Scotland by year of registration. Netherlands and China do not code as deaths infants who die before registration of births.[4,5] In Australia, vital events for nomadic aborigines are not recorded. In Sweden births need not be recorded for five years, and it is likely that many deaths are not recorded.[6]

Compilation of data in certain countries is by date of registration, not occurrence. Because deaths are more promptly reported than births—which may be years later—the IMR may appear to be greater than it is, just as the exclusion from registration of liveborn infants who die on the first day of life causes a "downward bias."

Definitions are sometimes tricky. Is the United Kingdom an entity? Occasionally it is shown as such on tabulations; other times its components are listed separately, leading to fluctuation in the rankings.

In order to be ranked, a country's population should be more than one million. Most countries are between three and 55 million, but Japan is 100 million, and the USA and Russia are over 200 million. The great population difference between the USA and Sweden (8 million) suggests the lack of comparability of such countries.

There seem to be two conflicting opinions of the validity of an IMR. One, that because of the variables, differences, errors, and lack of uniform specifications, a given IMR is suspect. The other, that although the health indices are crude measurements the shortcomings are acceptable because of the similarity of methods and definitions, and even if one could obtain complete and reliable data, the IMR would change only a few per cent points, not materially altering a country's ranking. At this point it seems useful to accept the second opinion, not only because it is championed by a few experts, but in order to get to important matters.

It is generally agreed that having no bearing on the position of the reporting nations are the ages of the mothers, the number of abortions, and extent of illegitimacy, the birth order of children, the improved infant death rates, and the high infant mortality in blacks in this country—the non-white infant death rate is 80 per cent greater than the white. If the non-white rate were adjusted to that of the white, the total death rate would change only 13 per cent, not enough to shift the rankings.[7-9]

Physician density is unrelated to the position of the nation. The United States, Belgium, and West Germany have higher IMR's and higher doctor-population ratios than the four countries with the lowest IMR's—Sweden, Norway, the Netherlands, and Finland. Sweden, with only 98 doctors per 100,000 population, has the lowest rate, and in comparison the United States has 143 doctors per 100,000. Pediatrician density is similar, the United States having almost twice as many as Sweden—7.1 as compared to 4 per 100,000. Thus, the quality of medical care seems to be unrelated.[10,11]

Sweden

After sifting through many studies it is surprising to find that there is a significant difference between Swedish and American newborns: there are proportionately fewer low-weight infants (those with a high risk) in Sweden (4 per cent of newborns) as compared to the USA (7 per cent). Furthermore, while the Swedish IMR has fallen about 100 per cent in 20 years, the death rate in prematures has not changed. It has been suggested that newborns are heavier in Sweden because of its lower birth rate and because of societal influence.[12]

We need to look more closely at Sweden. It is a homogeneous middle-class country with very few poor or rich people and no true minority groups. Ninety-nine per cent of its population are Lutheran. Although heavily industrialized, it has no slums and almost no unemployment. The Swedish growth rate is 0.6 per cent a year; that of the USA is one-third higher. The death rate in Sweden is 10 per 1,000; here it is 9.5. The birth rate in Sweden is 15 per 1,000; here it is 17.7 per 1,000.[13,14]

A third of the Swedish budget is allocated for social welfare programs. Maternal and child health services include "free" prenatal and obstetrical care based on compulsory health insurance paid for in part by the insured through his income tax, and by the employer and the government. Doctors and other health personnel receive 70 per cent of the outpatient fees. Pregnant women pay for only half the costs of such medicines as vitamins, iron and calcium. During pregnancy, heavy manual labor is prohibited. Women are permitted to leave their jobs six weeks before delivery and need not return until six months later. Cash maternity grants are available. A major effort is made to identify poor-risk mothers and those who might deliver low-weight babies, and to have them consult with specialists.

Training in obstetrics is emphasized. Public health nurses are drilled for five or more months in prenatal care and emergency obstetrical conditions. Midwives practice in hospitals, and in rural areas they provide first-line maternity care. (Even in Sweden it seems difficult to persuade physicians to settle in remote areas.) Maternity hospitals and homes have been constructed throughout the country, and all hospitals have specialized obstetric and pediatric facilities. In 1965, only 0.1 per cent of deliveries took place in homes.[12-14]

Illegitimate births are twice as frequent in Sweden as in our country, 13 as compared to 6.8 per cent, probably because many women believe they must prove their fertility before marriage. The Swedish government has eliminated the word "illegitimacy" from legal documents; "out-of-wedlock" is acceptable.

Some data show that Sweden, despite its dedication to goals of peace, elimination of poverty and hunger, and the pursuit of a high standard of living, has some unresolved problems. A nursing shortage exists because half of the nurses who marry do not return to their profession; if a nurse works, her income is added to that of her husband's and taxed as a single income; she has no financial incentive to continue in her field.[11] The suicide rate in Sweden is twice that of the United States, 20 as compared to 10 per 100,000.[15] Survival rates for Swedish women with cancer are a little poorer than for American women,[16] and mortality rates from tuberculosis, pneumonia, bronchitis and gastric ulcer are considerably higher in Sweden than in the United States.[17]

Isolated Facts

A few seemingly isolated facts seem worth reporting. Male infant death rates are thirty per cent higher than female, an indication of genetic determinants.[18,19] Racial influences are also known to exist. For example, a recent report describes the greater maturity of low-weight non-white babies as compared to low-weight white babies,[19] and another shows that in California there are lower death rates for Chinese, Japanese, and American Indian infants than for white infants. The death rate in these Indian infants was lower than in Indians born in other states, an unexplained finding.

In a brief review of infant deaths in the ruling families of Europe, it was shown that between 1900 and 1930 a death rate of 8 per 1,000 was achieved despite a much higher rate in the general population: in 1930 rates of 55 and 56 per 1,000 existed in Sweden and the United States.[21] One is led to assume that children of royalty (when removed from the threat of regicide) had certain advantages that the children of commoners did not have: constant attention, wet nursing, removal from unhealthy smog-laden atmospheres to sunny environments, and first-class food and housing. Or, perhaps, as wanted babies they had a better chance for survival than unwanted babies. Or were genetic influences at work?

There must be other associated factors. The one that seems indisputable is that more premature and low-weight infants are born to unmarried women, those in less favored social groups, and those who hold unskilled jobs—in both the United States and Sweden.[12] Studies in many countries confirm the association of low-weight infants with a high death rate and low socioeconomic status.[22] The most recent study from New York City noted an "unprecedented" decline in infant mortality between 1962 (27.3 per 1,000) and 1972 (20.1 per 1,000) achieved by a reduction in the fertility rate, in births to the very young and the relatively old, to mothers who already had many children, to those out-of-wedlock, and to women of low socioeconomic groups and those on public assistance. These were "achieved by a combination of significant and remarkable advances in medical technology and an impressive number of social advances. Family planning and safe abortions, which have become available to all women regardless of financial status, have played a decisive role . . ."[23]

". . . to Talk of Many Things"

The next time someone seeks my opinion about health indices, I will be ready. "The infant mortality rate is important, but only because it tells us how much progress a country makes from year to year. But it measures only one aspect of health—one country may have a higher infant death rate than another, but its tuberculosis or pneumonia mortality rate may be lower, so it is unfair to compare these countries with each other. I think it is important to recognize that our infant death rate has declined remarkably in the last few years, attesting to the strength of our health care system—astonishing when one considers the complex forces which affect survival."

Marcus J. Smith, MD
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Because of limitations of space, the list of references has been omitted. The complete list may be obtained from the author at 141 E. Palace Avenue, Santa Fe, 87501.

OUR COVER

The men who came West to where the gold was, knew the wealth was fabled, but undaunted by stories of how deep in the earth lay gold and silver, they strained to move equipment over high passes and up to heights like this, only to dig hundreds of feet down. Don Miller caught this mine in all its ruggedness.

Photocopy and Copyright

Under debate in the Judiciary Committee of the U.S. House of Representatives is a bill to restrict photocopy of library reference material (H.R. 2223). This proposed revision of the copyright law would prohibit the routine library practice of photocopy of scientific information. Obviously, by such a law the dissemination of scientific knowledge would be critically restricted. The interlibrary loan system would be abolished. Access of the scientific community to the literature would be dangerously curtailed.

At issue is redefinition of the concept of "fair use" by the copyright laws for journals. This issue has been under contention since 1968 when Williams and Wilkins filed suit against the National Institute of Health and the National Library of Medicine, charging that single photocopy of journal articles was a violation of the publishers' copyright. The government agreed that reduplication of individual articles was essential for dissemination of original knowledge and research findings. In 1973 the Court of Claims found in favor of the government and the present photocopy practice by a 4 to 3 vote. In February 1975 the U.S. Supreme Court did not overturn this decision. Now the matter is in a congressional committee for redefinition of the law. The issue involves not only medical journals but all publications.

Of course, the rights of authors and publishers must be protected. Certainly modern photocopy has the capability of easy and rapid reproduction of entire journals and books. But, obviously the access to scientific knowledge, or any knowledge, by individuals at every level of study, at every age, in every locality (metropolis, city, town, farm) must be maintained—and developed. Photocopy on a "systemic basis" as routinely conducted in the libraries seems essential to our scientific community and our educational process. "Fair use" must permit reproduction as necessary for the healthy development of our scientific base. There may be a problem of abuse or there may be discrimination against publishers and authors, but there must be legitimate photocopy dissemination of scientific information.

Does your congressman know that "systematic" reproduction of scientific material is essential to medical education and patient care?

Glucose tolerance testing:

Are we overdiagnosing diabetes mellitus?[*]

Robert N. Alsever, MD, Pueblo, Colorado

The glucose tolerance test is usually not necessary and is often misinterpreted.

Both the public and the medical profession know that diabetes mellitus affects a substantial portion of our population—almost four million. Likewise, both recognize that myocardial infarction, renal disease, peripheral vascular disease, and blindness are potential complications in diabetics—for which there are yet no cures. It is not surprising, therefore, that when a patient learns he is diabetic, both he and his family may experience fear and apprehension. Medical insurance companies share similar fears, and, as a result, most diabetics must pay increased insurance rates or are rejected for insurance.

Unfortunately, many patients carry the diagnosis of diabetes on the basis of improperly performed and interpreted tests of carbohydrate metabolism. Some patients are labeled "borderline" diabetics, but diabetes mellitus appears on their insurance record. It is incomprehensible that diabetes mellitus can be a borderline disease when no other medical diseases share such an unfortunate modifier. For instance, coronary artery disease, renal disease, hyperlipoproteinemias, hyperthroidsim, and pregnancy do not exist as "borderline" disorders. Such a cavalier attitude in making the diagnosis of diabetes mellitus, therefore, can be disastrous not only to the patient and his family, but also to the patient's medical and financial future.

Abnormal Glucose Tolerance Tests

Abnormal glucose tolerance tests are found in a high proportion of patients. They are called "abnormal" because they do not fit within two standard deviations of the mean glucose tolerance levels of the general population. Most are nondiabetic, examples of which are shown in Table 1. The first example, the commonly encountered flat glucose tolerance test, has no diagnostic meaning, whatsoever.[1] In fact, were we to consider this type of curve in terms of physiologic mechanisms, it would appear that such a patient would have perfect glucose homeostatic control. The second example represents a commonly seen delayed rise in the plasma glucose following the ingestion of oral glucose; such patients may represent those in whom delayed gastric emptying of the glucose load may occur or those who were poorly prepared for the glucose tolerance test. The third example demonstrates a curve with a high one hour glucose and normal values at 2, 3 and 4 hours; the fall in glucose concentration at 3 and 4 hours is a normal phenomenon when it occurs without simultaneous symptoms.[1] The fourth example demonstrates a patient with an abnormal 2 hour plasma glucose in whom the remainder of the glucose values are normal. This example specifically shows only that the lower limit or normal for plasma glucose at 3 to 4 hours

TABLE 1

Non-Diabetic Variations of Glucose Tolerance
Plasma Glucose MG/dl

Example	Fasting	1 Hour	2 Hours	3 Hours	4 Hours	5 Hours
1	69	82	75	80	72	70
2	100	125	160	120	80	100
3	80	240	138	55	60	80
4	72	160	145	92	38	65
5	90	160	135	100	120	85

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has been found to be 35 mg/dl;[1] it *does not* represent reactive hypoglycemia unless accompanied by symptoms thereof at the time the plasma specimen is obtained. The fifth example is a test with two glucose peaks, one at one hour and another at four hours. These examples all represent non-diabetic variations in glucose tolerance curves.

If examined carefully, most abnormal, and even many diabetic glucose tolerance curves, are caused by exogenous factors (Table 2).[1,2] Perhaps the most common of these are concurrent drug administration, hospitalization with prolonged bedrest and/or intercurring illness, and improper carbohydrate preparation. Since many drugs may alter glucose tolerance, it is wise to discontinue all possible medications prior to glucose tolerance testing. The most common offenders are shown in Table 2. The effect of drugs which we frequently may not consider is highlighted by the finding that the nicotine absorbed from smoking only two cigarettes prior to glucose tolerance testing may increase the blood glucose as much as 50% above the baseline value.[2] This effect may persist from one and a half to two hours. The effect of drugs, including the countless over-the-counter medications which a patient might consume prior to testing, should be considered in interpreting any test of carbohydrate tolerance.

Prolonged bedrest, itself, without intercurrent illness, has been shown to significantly alter glucose tolerance by impairing peripheral glucose uptake. This effect may last up to 7 days following re-ambulation.[3] The stress of illness or multiple procedures performed in a hospital setting should negate the results of any glucose tolerance test performed under these conditions. Hence, many diabetologists contend that *glucose tolerance testing should never be performed in a hospital setting.*

TABLE 2

Factors which may produce Glucose intolerance

- Dose and concentration of Glucose load
- Multiple venipuncture
- Time of day
- Bedrest
- Poor carbohydrate intake
- Starvation
- Stress (emotional or physical)
- Menstrual cycle (deterioration of Glucose tolerance days 7-18)
- Gastrointestinal diseases
- Active systemic disease
- Drugs
  - Diuretics, Diphenylhydantoin, Glucocorticoids, (topical or oral), Spironolactone, Diazoxide, Oral contraceptive agents, Estrogens, Nicotine, Caffeine, Salicylates, MAO inhibitors
- Hypokalemia
- Hypocalcemia
- Chronic illness (Renal failure, liver disease)
- Acromegaly
- Hypothyroidism
- Hyperthyroidism
- Pheochromocytoma
- Pregnancy

Finally, the patient's previous diet is a factor in regulating glucose tolerance. The absolute caloric intake does not appear to be the critical factor, but rather, the amount of carbohydrate consumed. It has been documented that daily carbohydrate intake of less than 150 grams prior to glucose tolerance testing will result in abnormal curves.[1] Thus, it is essential that every patient ingest 150 to 300 grams (preferably the latter) of carbohydrate prior to the glucose tolerance test. Following carbohydrate priming, the period of fasting before the performance of the glucose tolerance test also appears to be critical. The test should be initiated between 8:00 o'clock and 9:00 o'clock in the morning after a 12 hour overnight fast.

Obesity

The obese patient deserves special consideration, since he represents up to eighty per cent of the diabetic population. Frequently, obesity is associated with "diabetic" glucose tolerance curves which may occur in spite of abnormally high circulating insulin levels. Since these patients frequently demonstrate normal glucose tolerance following weight loss, we must ask the question: Are these patients truly diabetic? To label them as such permanently mars their medical record for health insurance, life insurance, and employment, even when their glucose tolerance returns to normal with weight loss. Mice enjoy a far better fate than man in this regard. Scientists have described a certain strain of mice called "genetic obese *hyperglycemic* mice" rather than "genetic obese *diabetic* mice". Why should not man be so fortunate?

Criteria for Diagnosis

Further compounding the problems of glucose tolerance interpretation are the many criteria which now exist for the diagnosis of diabetes mellitus. Four of these sets of criteria are shown in Table 3.[1,4,5] Careful examination shows that a patient could be diabetic by one set of criteria and yet not by another. The author prefers the criteria of Fajans and Conn since all plasma glucose values following the ingestion of

TABLE 3

Criteria for diagnosis of diabetes mellitus by oral glucose administration*

		Plasma glucose (mg/dl)
Fajans and Conn	1 Hour	>185
1.75 g glucose/kg ideal body weight	1-½ Hour	>165
	2 Hour	>140
Diabetes=all 3 values abnormal		
Wilkerson	Fasting	>130(1 point)
100 g glucose to all patients	1 Hour	>195(½ point)
	2 Hour	>140(½ point)
	3 Hour	>130(1 point)
Diabetes=2 points		
University Group Diabetes Program		
30 g glucose/m^2		
Diabetes=sum of fasting, 1 Hour 2 Hour, and 3 Hour more than 600 mg/dl		
ADA		
40 g glucose/m^2	Fasting	>115
	1 Hour	>185
	½ Hour	>165
	2 Hour	>140
Diabetes=elevated fasting or all 3 postprandial values abnormal		

*Do not apply during pregnancy

the glucose load must be abnormal for the diagnosis of diabetes mellitus to be made. Moreover, the amount of glucose administered is based on the ideal body weight rather than a random 100 gram carbohydrate load regardless of the patient's size. Perhaps more liberal diagnostic criteria are those of the University Group Diabetes Program.[1,4] Regardless of which set of criteria are used in testing, it is essential that the correct amount of glucose be administered which corresponds to the set of criteria being used. In interpreting the test, consideration should probably be given to age, since glucose or carbohydrate tolerance apparently deteriorates with age as a normal phenomenon.[5] It has been suggested, therefore, that 10 mg/dl be added to the upper limit of normal of each postprandial glucose value for each decade of life over 50 years.[5]

Approach to Diagnosis

In the vast majority of true diabetics the diagnosis can be made *without* the use of a glucose tolerance test. In all patients in whom the diagnosis is suspected or in whom diabetes screening is desired, the following logical approach should be followed:

ONE: Determine plasma glucose in either fasting or random specimens. If a fasting plasma glucose is greater than 130 mg/dl or a random sugar is above 195 mg/dl, a diagnosis of diabetes is clearly evident and no further testing need by done, providing that care has been taken to exclude those factors which may alter this value as discussed previously.

TWO: If these results are inconclusive or further screening is desired, a plasma glucose should be obtained after ingestion of a meal containing at least 75 grams of carbohydrate. Prior to testing, 3 days of carbohydrate priming, as discussed previously, are necessary. The patient is then instructed to fast for 12 hours overnight, consume a breakfast containing at least 75 grams of carbohydrate, and report to the laboratory for a plasma glucose determination exactly 2 hours after completing the meal. If this value is less than 140 mg/dl, further testing is not indicated. If the 2 hour value is greater than 140 mg/dl but less than 160 mg/dl, a glucose tolerance test is probably indicated. If the 2 hour value is greater than 160 mg/dl and the fasting glucose is elevated, diabetes mellitus is present and no further testing is necessary.

Glucose Tolerance Tests

After the above diagnostic steps have been carried out only a few patients will require glucose tolerance testing to arrive at the diagnosis of diabetes mellitus. Again, prior to testing, 3 days of carbohydrate priming must be carried out and the patient removed from any factors (Table 2) which might be associated with deterioration of glucose tolerance. The glucose tolerance test should then be performed according to any of the procedures and criteria outlined in Table 3. The criteria for determination of diabetes must be rigidly adhered to and a diagnosis of diabetes mellitus must not be made unless *all criteria are met.* It cannot be overemphasized that a glucose tolerance test is *never* indicated in the presence of fasting hyperglycemia.

The rapid intravenous glucose tolerance test is rarely if ever indicated in clinical medicine.[6] If deemed necessary by the physician it should be performed according to well standardized methods which are beyond the purview of this paper.[1] However, in interpreting the results, the physician should be aware that the test correlates poorly with the oral glucose tolerance test and that patients shown to meet clearcut criteria for diabetes mellitus by one method may have normal results by another. Hence, its use in clinical medicine must be limited.

Summary

Abnormal glucose tolerance tests are common findings in clinical medicine and do not indicate the presence of diabetes mellitus. At present the oral glucose tolerance test is being overutilized when fasting, and 2 hour postprandial plasma glucose determinations will suffice in most instances. In interpreting any plasma glucose concentrations, consideration must be given to those factors which may alter the circulating glucose level. In rare instances a glucose tolerance test may be indicated. In such cases, careful attention to factors which alter the results of the test and strict adherence to a single group of diagnostic criteria should reduce the inappropriate diagnosis of diabetes mellitus and thereby benefit both physician and patient.

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UNIVERSITY OF COLORADO
MEDICAL CENTER
UPPER EXTREMITY AMPUTEE CLINIC

The University of Colorado Medical Center has recently established an Upper Extremity Amputee Clinic that meets the 2nd and 3rd Wednesdays of each month at 10:00 a.m. It is staffed by a physician, therapist, prosthetist, nurse and other appropriate personnel. Patients may be referred to this service by contacting Mrs. Diana Mattox — (303) 394-8718 or through the Therapy Department, Mrs. Bonnie Olivett — (303) 394-8303.

Patients are accepted by referral from physicians or appropriate agencies.

Endoscopy in upper gastrointestinal tract bleeding*

Klaus Anselm, MD and Rodney C. Dwyer, MD, Pueblo, Colorado

Endoscopy is recommended as the initial procedure for diagnosis of site and cause of upper gastrointestinal bleeding.

The diagnostic approach to patients with upper gastrointestinal bleeding has gone through several forms during the past decades. While upper gastrointestinal barium studies previously offered the only means of diagnosis the present general acceptance of endoscopy, proposed in 1969 as a vigorous diagnostic approach,[1] has brought about a dramatic change. With the improvement of endoscopic instruments and the appearance of fiberoptic technics, endoscopic accuracy has substantially improved.[2,3] Furthermore, advent of the long forward viewing instrument,[3,4] allowing examination of the esophagus, stomach, and duodenum as a single procedure has reduced the risk to the patient. The frequent occurence of hemorrhagic or erosive mucosal disease has become apparent,[5] and the per cent of patients bleeding from unknown sources has gradually decreased. With better visualization of the upper gastrointestinal tract, the frequent concurrence of several potential bleeding sites has been recognized.[3] This report concerns our experience with one hundred bleeding patients consecutively examined.

Methods

One hundred consecutive patients admitted with upper gastrointestinal bleeding to three institutions (St. Mary Corwin Hospital, Parkview Episcopal Hospital, and Colorado State Hospital) were examined with the Olympus Gastro-Duodenoscope (GIF). This fiberscope has a total length of 105 centimeters and a diameter of 13 millimeters. It has a forward viewing lens which can be cleaned by a water jet, channels for air insufflation, suction and passage of a biopsy forceps or cytology brush. It has flexibility allowing visualization of the upper gastrointestinal tract up to and including the second portion of the duodenum.

When possible the examination was performed during the first 48 hours after bleeding or admission, but was postponed when necessary until vital signs had stabilized. Ice water lavage was performed prior to endoscopy in patients with massive bleeding. The examination was normally performed in a special treatment room, occasionally in the emergency room, intensive care unit or on the ward. Five to 20 mgs of diazepam were injected intravenously before the examination.

Results

In ninety-six of one hundred patients endoscopically examined, the source of bleeding was identified (Table 1). The procedure was well tolerated by all patients, with no morbidity or mortality attributed to it.

In fifty-nine patients evidence of peptic ulcer disease was found while sixty-nine patients presented with the endoscopic appearance of diffuse erosive mucosal disease. Of the latter, 12

TABLE 1

Endoscopic Diagnoses in 100 Bleeding Patients

Gastric Ulcer	39
Duodenal Ulcer	20
Hemorrhagic Gastritis	36
Hemorrhagic Duodenitis	17
Hemorrhagic Esophagitis	16
Mallory-Weiss Syndrome	8
Esophageal Varices	7
Gastric Carcinoma	4
Duodenal Carcinoma	1
Not Diagnostic	4

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TABLE 2

Incidence of Multiple Diagnoses

Single Lesion	47
Two Lesions	34
Three Lesions	12
Four Lesions	3

patients had more than one part of the gastrointestinal tract involved, six had combined hemorrhagic gastritis and duodenitis. Four of 16 patients with hemorrhagic esophagitis had associated hemorrhagic duodenitis, one patient had hemorrhagic esophagitis, gastritis, and duodenitis. Esophageal varices were seen in seven patients, although in only one found to be the source of bleeding. Eight patients had Mallory-Weiss Syndrome, five carcinoma of the stomach or duodenum.

In four patients the endoscopic examination was not diagnostic. One patient had a large amount of retained barium from an earlier upper gastrointestinal X-ray study, two patients had a large amount of fresh and old blood within the gastric lumen, making proper examination impossible, and in one patient the examination was considered normal.

The association of several potential bleeding sites was noted in 50 patients (Tables 1 and 2). Thirty-five patients had two potential bleeding lesions, twelve had three, and three patients had four different potential bleeding sites. Of these the frequent association of gastric ulcers, hemorrhagic gastritis, and duodenal ulcers with one another, and other bleeding sites is apparent from Table 3.

Roentgenologic examination of the upper gastrointestinal tract was performed in fifty patients (Table 4). In 22 the study was considered normal, while in 12 the roentgenographic diagnosis concurred with the endoscopic findings. In 16 other patients the examination was abnormal but not diagnostic for the source of bleeding; in seven of these hiatus hernia was the only finding while in four others only antral deformity was detected.

TABLE 3

Frequently Concurring Endoscopic Findings

A. Gastric Ulcer	
Single Ulcers	13
Multiple Ulcers	7
Ulcer (s) with Hemorrhagic Gastritis	6
Ulcer (s) with Duodenal Ulcer	5
B. Hemorrhagic Gastritis	
Hemorrhagic Gastritis Only	21
Hemorrhagic Gastritis with Gastric Ulcer	6
Hemorrhagic Gastritis with Duodenal Ulcer	4
Hemorrhagic Gastritis with Mallory-Weiss Syndrome	4
Hemorrhagic Gastritis with Hemorrhagic Duodenitis	2
C. Duodenal Ulcer	
Duodenal Ulcer Only	7
Duodenal Ulcer with Duodenitis	6
Duodenal Ulcer with Hemorrhagic Gastritis	4
Duodenal Ulcer with Gastric Ulcer	5
Duodenal Ulcer with Mallory-Weiss Syndrome	2

TABLE 4

Radiological Diagnoses in 50 Patients with Bleeding

Normal Study	22
Correct Diagnosis	12
Abnormal, but not Diagnostic	16

Discussion

The value of endoscopy for the evaluation of the patient with upper gastrointestinal bleeding is well recognized. The vigorous diagnostic approach proposed by Palmer[1] has with a few modifications stood the test of time. Improvement of endoscopic technic and the advent of fiberendoscopy with the new esophago-gastro-duodenoscopes or pandendoscopes has decreased discomfort to the patient and improved diagnostic accuracy.[2-4] Endoscopic documentation of duodenal ulcers and hemorrhagic duodenitis has decreased the per cent of patients bleeding from unknown sources.[4]

The present study concurs with results of others, but a few additional points of interest are apparent. A larger per cent of patients has been found with hemorrhagic mucosal disease. Further, a high incidence of multiple potential bleeding sites found during a single examination is recognized, and a larger than usual number of patients with Mallory-Weiss Syndrome has been found.

Palmer[1] already emphasized the importance of multiple potential bleeding sites seen during endoscopy, finding 40 per cent of patients with a known potential bleeding source to bleed from a different lesion. Our results concur with this. Forty-nine per cent of patients had more than one potential bleeding site detected by endoscopy.

The high incidence of Mallory-Weiss Syndrome, 9 per cent, has been surprising but not unexpected. While in many reports the incidence has ranged from 2 to 6 per cent,[2-4,6] new instruments and technics have recently yielded better results.[7] None of our patients with Mallory-Weiss Syndrome required surgery, confirming the contention that it is a more benign entity than originally described.[7]

In recent years the practical value of early endoscopy in patients with upper gastrointestinal bleeding has been challenged on the ground that it has failed to influence or improve survival of patients. It appears, however, that endoscopic detection of multiple abnormal findings more than justifies the procedure, particularly in patients with known active peptic ulcer disease, found bleeding from associated hemorrhagic gastritis or duodenitis. Recurrent upper gastrointestinal bleeding is often an indication for elective surgery in patients with peptic ulcer disease. Recognition of other bleeding sources will be of help to put the patients' problems in the proper perspective. We recommend that panendoscopy be carried out as soon as possible after hospitalization and when vital signs are stable, prior to barium study of the upper gastrointestinal tract.

Summary

One hundred consecutive patients admitted with bleeding from the upper gastrointestinal tract were examined with the forward viewing gastro-duodenoscope. The site of bleeding was detected in 96 patients. A high incidence of multiple potential bleeding sites was found in many patients (49%). Eight patients were observed to bleed from Mallory-Weiss Syndrome. It is recommended that fiber-endoscopy be performed as soon as feasible in patients with upper gastrointestinal bleeding.

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Adriamycin in advanced childhood malignancy*

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This drug is useful in a wide spectrum of malignancy.

TREATMENT OPTIONS HAVE BEEN DISAPPOINTING for the child with advanced cancer who is unresponsive to standard modes of therapy. Adriamycin (ADRA) (NSC-123127) is a cytotoxic antibiotic first introduced in 1967 and is a close chemical analog of Daunomycin (NSC-82151). The latter agent has previously been reported to be effective for the remission induction of acute leukemia and the regression of certain tumors.[1-4] Recently, several articles have appeared citing the response of a broad cross-section of malignancies to ADRA.[5-11] This preliminary report records the clinical experience with ADRA administered to 54 patients, 39 with solid tumor malignancies, and 15 with childhood leukemia.

Methods

All patients were treated at The Children's Hospital Oncology Center in Denver and received ADRA in accordance with a phase II chemotherapy evaluation protocol approved by the National Cancer Institute. Each patient had locally extensive or metastatic malignancy, except for 8 patients with bone tumors in which ADRA was used as adjuvant therapy. Those having childhood leukemia had initially achieved remission with Vincristine, Cyclophosphamide, Daunomycin, and Prednisone or L-Asparaginase. All patients had suffered two or more marrow relapses treated with a variety of anti-leukemic agents.

Status of disease was carefully monitored by serial clinical, radiographs, and laboratory examinations. Laboratory parameters included complete blood count, phase platelet count, blood urea nitrogen, serum creatinine, urinalysis, urinary catecholamines or VMA spot test (neuroblastoma), or alphafetoprotein, lactic acid dehydrogenase (LDH), and SGOT. Electrocardiographic, biochemical, and hematologic parameters were assessed before, during, and after therapy as a measure of tumor response and of drug toxicity. Pulmonary metastatic lesions were demonstrated by four-way X ray view of the chest. Serial two-dimensional measurements of well defined metastatic lesions were made on the view most clearly demonstrating the lesion. Radioisotope tools such as the Te99M bone scan, and Ga67 liver scan provided sensitive detection of non-pulmonary metastatic disease. Patients' subjective responses following administration of ADRA were also recorded. New data shows that the echocardiogram taken serially with calculation of the ejection function is the most sensitive way to monitor Adriamycin cardiac toxicity, and patients have been followed in that fashion.

Objective responses were defined as follows: complete remission (CR)—total disappearance of signs of malignancy; partial remission (PR)—signs or a net decrease in tumor mass; static (S)—no net change or a definitely attenuated growth rate of the tumor mass, or if ADRA was used as adjuvant therapy, a metastatic-free interval; and no response (NR)—clear-cut progression of malignant growth. Leukemic responses were evaluated according to criteria described by Basel.[13]

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* From the Denver Children's Hospital, Oncology Center, Denver. This paper was presented at a meeting of the American Association of Cancer Research, Atlantic City, 1973, by Dr. Mitchell. The investigation was supported in part by the National Cancer Institute Grant #5 PO2 CA 12247-04. Address reprint request to Children's Hospital, Oncology Center, 1056 East Nineteenth Avenue, Denver, Colorado 80218. Dr. Holton was formerly Director, Pediatric Oncology Center, Denver, and Director, Colorado Regional Cancer Center. Dr. Mitchell was formerly Oncology Fellow, Denver Children's Hospital and Fitzsimons Army Medical Center and is presently at Tripler Army Hospital, Honolulu. Ms. Ewenstein serves in the Oncology Center, Denver.

Adriamycin is administered at this center according to the following dosage schedules. Solid tumor patients have been given either 40 mg/M^2 IV every 7 days or 60 - 120 mg/M^2 IV every 21 days. Selection between these two schedules was made by individual physicians considering the bone marrow reserve, general physical condition, and anticipated psychologic tolerance of the patient and parents for toxic side effects. The first six acute leukemia patients studied received 0.5 mg/Kg IV daily for a total of 2 to 3 mg/Kg per course according to Tan, et al.[17] The subsequent nine leukemia patients received 35 to 40 mg/M^2 IV weekly based on new data showing a prolonged half-life for ADRA in the body. This later schedule was more acceptable to the children, because of fewer venipunctures. A total accumulative dose of 550 mg/M^2 was not exceeded in any patient, because of reported dose-related cardiac toxicity.

Results

Thirty-nine patients with solid tumor malignancies have received ADRA at The Children's Hospital since August, 1971. Their ages ranged from 8 months to 28 years.

A total of 30 out of 39 patients had apparent clinical response to ADRA (Table 1). Complete remission was achieved in four patients, partial remission was noted in fourteen patients, disease remained static in twelve, seven did not respond, and 2 were not evaluable.

In osteogenic sarcoma the drug was used as adjuvant therapy to surgical amputation or radiation therapy in eight patients with no evidence of metastases in this group at 3 years 4 months, 2 years, 1 year 6 months, 1 year 3 months, 9 months, 5 months, 3 months, and 2 months. Four patients presented with osteogenic sarcoma metastatic to the lungs or bone. In this group, two had static disease for 8 and 13 weeks, then progressed. One had partial regression with a decrease in lesions for several months and one had no response.

Of the eight patients with rhabdomyosarcoma, all had received prior therapy with Vincristine, Dactinomycin and Cytoxan and showed progression. There were no complete responses, but four partial regressions, two static disease responses, one non-responder, and one patient died with extensive disease after one dose of ADRA.

The four patients with neuroblastoma were all over 2 years with advanced disease that had progressed during Vincristine and Cytoxan therapy. No complete responses were noted, but one partial, one static, and two non-responders were observed.

A heterogenous group of solid tumors that had progressed on conventional therapy was also treated. There were four complete responses—one embryonal carcinoma, one mixed sarcoma and 2 Wilms' tumors. Eight partial responses were noted: two in Hodgkin's disease, one in Wilms', one hepatic carcinoma, one hepatoblastoma, one undifferentiated sarcoma, one angiosarcoma, and one embryonal carcinoma. No response was noted in three patients with leiomyosarcoma, mesenchymona, and Wilms' tumor.

Fifteen patients with acute leukemia, fourteen lymphocytic and one myelocytic, received ADRA. The group had experienced 2 to 4 relapses. ADRA was given as a single agent in accordance with early phase II protocol procedure. No child in this group achieved remission and in only one instance was the number of blasts reduced (Table 1). Seven of these fifteen patients did receive Daunomycin as a part of a previous induction regimen, and this may account partially for the lack of response observed. In each patient, ADRA was discontinued after two or more doses because of progressive disease. Toxicity was moderate in this group and was comparable to that seen using 40 mg/M^2 IV weekly in solid tumor patients.

Toxicity

The clinical toxicity of ADRA in the tumor patients is outlined in Table 2. Alopecia and leucopenia occurred in all patients who received a full course of therapy. Alopecia persisted as long as ADRA was administered. The mean nadir white blood count was 2200/mm^3 with a range of 500 to 3600. This nadir was reached on average day 9 with a range of 7 to 14 days. Nausea, vomiting, stomatitis, and moderately severe infection were frequent. Vomiting typically began several hours after drug injection and persisted 1 to 3 days. Anorexia persisted for a longer period coinciding with stomatitis with a resultant moderate weight loss. A general trend was observed indicating that gastrointestinal symptoms improve considerably with each succeeding dose. Peak stomatitis consistently coincided with the nadir of leucopenia. However, stomatitis seldom accompanied leucopenia at the lower 40 mg/M^2 dose. No appreciable alterations in tests of liver and renal function were observed. Six patients received radiation concurrently with ADRA. Five of the six had accentuated radiation effects consisting of moderate burns and blistering of the skin or mucosa. Electrocardiographic changes were detected in four other patients. Two patients developed signs of congestive heart failure; one had received radiation therapy to the spine, and had tumor in the superior vena cava at autopsy. No toxic heart damage was noted microscopically. The other patient subsequently responded to diuretics and digoxin. Neither patient received over 500 mg/M^2 of ADRA.[15-18] Borderline T-wave changes were first seen in one patient when her accumulative dose reached 370 mg/M^2. Another 100 mg/M^2 was given with no change. The other patient's ECG revealed tachycardia, ST and T wave changes suggestive of anterior myocardial ischemia, and a large S in lead V-6 suggesting right ventricular hypertrophy. This patient had rhabdomyosarcoma involving the mediastinum and had received 2,000R to the mass. Her ECG changes were in no way clearly attributable to ADRA. She subsequently expired from extensive pulmonary metastatic disease 6 weeks later. One patient died with overwhelming pneumonitis, presumably viral.

There was significantly greater incidence of thrombocytopenia, nausea, vomiting, stomatitis, and serious infection at the higher dose. The mean nadir for the white blood count was only slightly lower for the 120 mg/M^2 dose. The nadir occurred between the 7th and 14th day with each schedule. The nadir frequently coincided with the next dose on the low dose weekly schedule, leading to frequent modification or skipping of doses. On the other hand, with the higher dose given every 3 weeks, the white count usually recovered prior to the next dose. The high dose schedule therefore occasionally required modification.

Discussion

The patients reported represent a wide cross-section of neoplasia in childhood and early adulthood. The numbers of each tumor cell type are small and no conclusions can be derived about the relative efficacy of ADRA versus individual malignancies. The overall response of those patients with advanced solid tumors is encouraging. Slight superiority of the high dose schedule relative to the low dose schedule should be demonstrated in four patients who responded at the high dose after failing on the lower dose. Toxic manifestations of the high dose were more severe and discomforting for the patient. Thus far, no fatal drug toxicity has occurred. The current recommended maximal accumulative total dose of 550 mg/M^2 was not exceeded.

As a single agent in our patients, ADRA did not compare favorably with Daunomycin for remission induction of advanced acute leukemia. Remission induction rates for Daunomycin alone are reported to be 18 to 39 per cent.[2] Daunomycin in combination with Prednisone reportedly induces remission in 60 to 80 per cent of acute leukemia.[7,13]

The efficacy of ADRA as an induction agent remains to be shown, and the lack of response in our group may reflect a cross-resistance with Daunomycin used earlier in treatment.

Our experience suggests that ADRA is a useful chemotherapeutic agent in the management of disseminated solid tumors refractory to standard treatment. A prophylactic role for ADRA in newly diagnosed osteosarcoma, and incorporation of ADRA into combination chemotherapy for initial treatment of advanced acute leukemia, Ewing's sarcoma, rhabdomyosarcoma, neuroblastoma, Wilms' tumor, and embryonal carcinoma are currently under investigation. Our leukemic data supports the work in experimental systems that shows cross resistance between Adriamycin and Daunomycin.

Summary

Fifty-four patients with advanced neoplastic disease were treated with a new anti-tumor antibiotic, Adriamycin. Four had complete responses, 14 had partial response, 12 had static disease, 7 did not respond, and 2 were not evaluable. Adriamycin is a useful agent in a wide spectrum of malignancy. It is now employed earlier in the chemotherapy programs based upon encouraging results in advanced disease.

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Continuous somatic analgesia

*An Alternate for Postoperative Analgesia**

Stuart L. Smith, MD, Wheat Ridge, Colorado

A new, practical method of limiting epigastric postoperative pain while improving pulmonary ventilation is described.

This paper describes a method of controlling postoperative abdominal pain with an apparent improvement in ventilation. Analgesia was obtained by instilling lidocaine solution through perforated tubes placed across the somatic nerves before closure of the incisions. Anatomically, the 71 operations represented were: 15 gastric; 35 biliary; one small bowel; 11 colon; one renal; five abdominal wall; one lumbar sympathetic nerves; one appendix; and one spleen. Timed pulmonary function data were recorded in 42 of the cases and postoperative arterial oxygen saturations are reported for 34 patients. The use of lidocaine concurrent with barbiturates and ataractics was documented in all cases. Contrasted are postoperative data from 12 control patients, and postoperative arterial blood gases in another 12 controls, all medicated with conventional narcotics alone.

Altogether, the cases cited represent 95 consecutive adult patients from the author's private practice who underwent elective epigastric incisions between 1971 and 1974. These operations were performed at an altitude of 5442 feet where the normal arterial oxygen is 65-70 torr.

History

Historically, surgeons have recognized the special pulmonary complications limiting the success of upper abdominal procedures.[10,18,24,6] Intercostal nerve block for upper abdominal operations was described and was associated with improved vital capacity.[5,28,20] A variety of local anesthetics have been injected around or into wounds,[11,9] as paravertebral block,[15] and intravenously.[23,7] In 1957, Anscombe[3] reviewed the literature and concluded the major postoperative pulmonary problems were mechanical and secondary to reduced lung capacity, as well as to reduced inspiratory and expiratory flow rates. These, in turn, were secondary to spasm of the muscles of the incision, especially those innervated by T-6 to T-12.

Procedure

Sterile conventional tubing with perforations at the trailing end was threaded onto a 14 inch stylet measuring one-eighth inch in diameter and curved to follow the elliptical planes of the abdominal wall.†

The ventral primary divisions of the sixth through the twelfth thoracic nerves lie on the ventral surface of the transversus abdominis muscle, and on the posterior layer of the rectus sheath, supplying the adjacent peritoneal and cutaneous surfaces,[1,4,16] (Fig. 1) With the operation complete, the assistant maintains gentle traction on transversalis fascia and peritoneum. A tiny stab wound is made lateral to the lower level of the incision to introduce the tip of the stylet. As the outer hand forces the stylet cephalad through the abdominal wall, the stylet can be clearly felt by the intraabdominal hand, advancing upon the transversus fascia. Placement in the rectus sheath requires "popping" the stylet through the anterior rectus fascia which is considerably tougher than external and internal oblique muscles. Thus the stylet and

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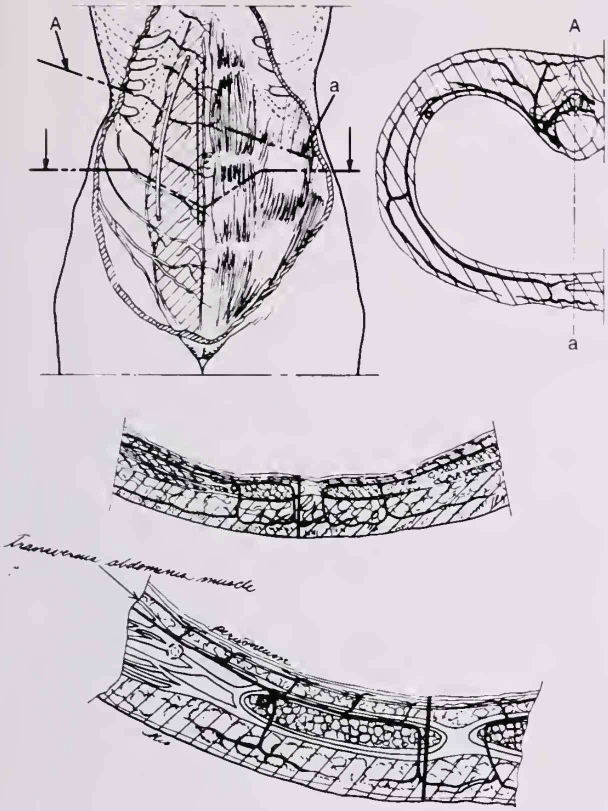


Fig. 1. Tubing in relation to somatic nerves.

tubing are kept out of the incision, and out of the abdominal cavity, and at the plane of transversus fascia to intercept the somatic nerves with the perforated section of the tubing. The tip of the stylet is forced out through a second tiny stab wound, the tubing is drawn through, the trailing end trimmed and the emerging portion sutured in place. (Fig. 2) Appropriate adaptors are attached to permit prompt delivery of lidocaine with heparin, 1 mg. per cc. The result is a sterile closed system which can be incorporated in the dressings after wound closure.

Commercial lidocaine without epinephrine was used, usually in one per cent concentration. Early in the study, eight to 20 cc of this solution were hand-injected, and microdrip infusion was tried. It has been more accurate, in most cases, to deliver the analgesic agent continuously using a commercial pump. With this latter method, analgesic infusion per hour has been kept from five to 20 cc, including one or two cc for flushing each tube every hour. Lidocaine dosage therefore is well within prescribed limits. Other medications concurrent with lidocaine include barbiturate and hydroxazine hydrochloride for sleep or paresthesias.

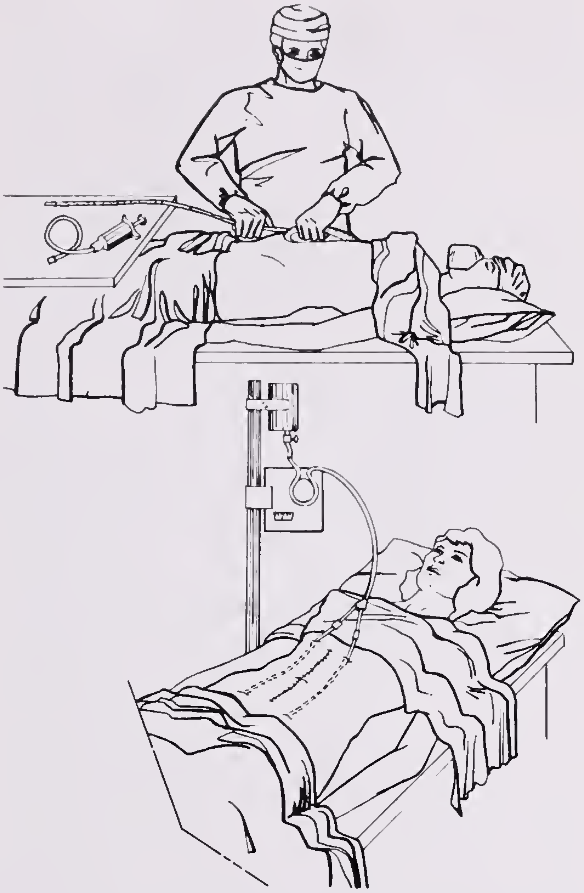


Fig. 2. Placement of tubing and attachment of pump.

Results

Requirement of postoperative narcotic is eliminated or reduced. Twenty-two patients of the author's prior to this study (comprising six gastric, four colon, and 12 biliary operations) averaged slightly more than 15 narcotic injections postoperatively. This is also the average narcotic usage for patients of several surgeons in the same medical center after gastric and biliary operations. In the 71 patients using the system of continuous somatic analgesia postoperatively, 61, or 86 per cent, needed no narcotics postoperatively. Of the remaining 10 patients, five needed a single narcotic injection, one received two injections, two received three injections, and one received five injections.

In cases undergoing high retroperitoneal dissection (vagotomy, hiatus herniorrhaphy, and common duct exploration), patients sometimes complained of dorsal pain. This usually occurred in the recovery room and responded to a single dose of narcotic. Drain sites lateral to the

TABLE 1

			1st day	3rd day
1	Lidocaine Analgesia	1973	58.5%	69.8%
2	Author's controls	1973	55.1	58.8
3	Latimer	1971	38	50
4	Beecher	1933	42	48
5	Powers	1928	34	48
6	Head	1927	20	30
7	Churchill	1927	25	33

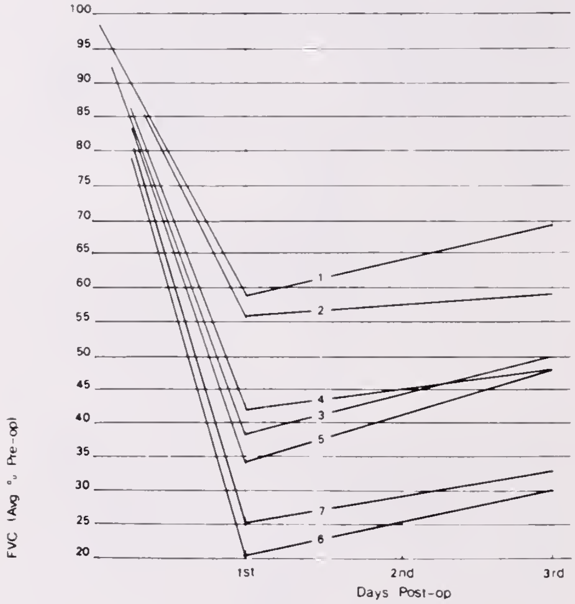
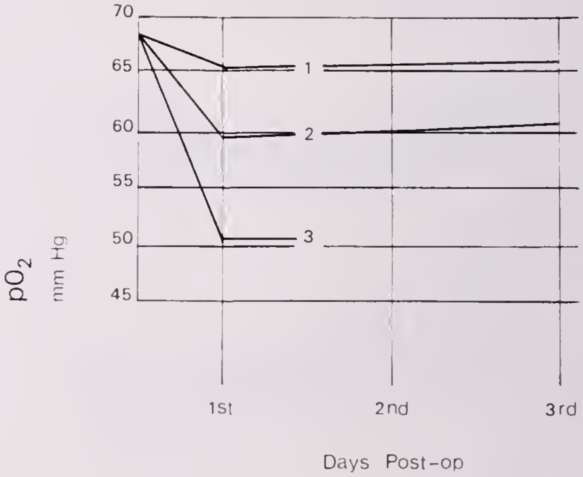


TABLE 2

Arterial Oxygen Levels Averaged (room air)

1 34 with lidocaine and normal PFT
2 20 with lidocaine and FEV_1/FVC under 75%
3 conventional narcotics controls
    3 gastric
    4 biliary
    5 colons



zone of analgesia did not represent a significant source of postoperative pain. Modest amounts of hydroxyzine hydrochloride controlled paresthesias and normal doses of barbiturate were used for sleep. The apparatus was left in place until patients were able to take oral medication—usually two to four days. Patient acceptance has been uniformly good and nursing notes reflect satisfaction in managing these non-narcotized subjects. They breathed freely as if the afferent neuronal limb of the splinting mechanism had been interrupted.

Pulmonary function was analyzed. Measurements* were made by the same technician, with patients sitting or standing at the bedside prior to operation and on the first and third days after operation. Postoperative results have been recorded as per cent of preoperative values. The average Forced Vital Capacity of 42 patients in the lidocaine series was found to be 58.3 per cent of preoperative value on the first postoperative day, and 68.7 per cent of preoperative level on the third postoperative day. Twelve controls averaged 55.1 per cent, and 58.1 per cent of preoperative values on the first and third postoperative days respectively. (Table 1) Twenty patients undergoing 21 operations had preoperative FEV_1/FVC equal to less than 75 per cent. This arbitrary level has been set to indicate some form of Pulmonary deficiency. Under continuous lidocaine analgesia they did surprisingly well, averaging 71.1 per cent of their preoperative FEV_1 on the first day after operation. By the third day, this average had risen slightly to 76.6 per cent of preoperative value.

Forced Vital Capacity and one-second Forced Expiratory Volumes previously have not been reported as high as 58 per cent of preoperative level on the first and third days after operations in the epigastrium. The high level of controls is unexplained but may partly reflect the facts that only one patient smoked, none had chronic pulmonary disease, and they averaged only 46 years of age. Latimer[19] has shown an initial 65 per cent drop in postoperative pulmonary functions and an 87-88 percent oxygen saturation through the first postoperative week in operations performed at

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about the same altitude in Salt Lake City, Utah.

Arterial blood gas determinations were made on 34 patients receiving lidocaine and breathing room air. The arterial oxygen saturation averaged 65 and 66 torr on the first and third postoperative days respectively. The normal arterial oxygen range is 65-70 torr at an altitude of 5442 feet. In the 20 of these patients whose preoperative assessment indicated a pulmonary disorder (i.e., FEV_1/FVC under 75 per cent), the average arterial oxygen on room air was 59 torr on the first postoperative day and 61 torr on the third postoperative day. Twelve control cases received only traditional intramuscular narcotics postoperatively. Their average preoperative arterial oxygen of 68 torr fell to an average of 51 torr on the first postoperative day. (Table 2)

Hypoxemia is expected after upper abdominal surgery.[12,17,21,22,25] However, the arterial oxygen in patients undergoing continuous somatic nerve analgesia averaged, as stated above, 65 and 66 torr on the first and third days postoperative, respectively. These values are very nearly normal for preoperative arterial oxygen saturation in Denver, Colorado, where the normal arterial oxygen is 65-70 torr. Moreover, the 20 patients whose preoperative FEV_1/FVC was under 75 per cent averaged a postoperative arterial oxygen of 59 torr and 61 torr on the first and third days.

Complications

There was no wound infection or hemorrhage and none of the tubing sites of tubes themselves gave any evidence of infection. There were also no patients with fever in excess of 101°F. which lasted more than 24 hours. One patient was dependent on demerol (30 doses in two weeks) prior to his hiatus herniorrhaphy, vagotomy, and pyloroplasty, and his demands did represent a nursing problem on the ward. One patient was ruled a failure during the first day due to no relief and was switched to conventional narcotics. One patient with chronic obstructive pulmonary disease underwent cholecystectomy and developed gastric dilation postoperatively, requiring intubation.

Lidocaine Toxicity

The adverse effects of lidocaine are systemic and usually due to high plasma levels caused by exceeding the recommended dosage level.[2] Cardiovascular depression, which may occur simultaneously with central nervous system effects, may be overlooked because of the more dramatic convulsions. Allergy to local anesthetics including lidocaine is rare; however, allergy to the methylparaben preservative in lidocaine is documented.[13]

Accurate dosages of lidocaine have been correlated with clinical effects and blood levels.[8,14,26] The prolonged use of four mg. per minute of intravenously given lidocaine is safe in a 70-kilogram adult and is in common use. However, tolerance to local anesthetic agents varies with the patient's metabolic status. The actual blood levels of lidocaine with this prolonged continuous administration need to be documented in relation to specific central nervous system effects. Adriani[2] has emphasized that myocardial disease, electrolyte imbalance, acidosis, anemia or hepatic failure may be responsible for an adverse reaction to a dose which otherwise would be safe. Heart block is a relative contraindication to the use of lidocaine. In vitro animal studies have shown lidocaine to be rapidly metabolized aerobically on passage through the liver.[27]

Summary

A new, practical method of limiting epigastric postoperative pain has been described. The method employs a continuous lidocaine analgesia of the abdominal wall following epigastric incisions. Lidocaine was delivered through perforated tubing positioned, with the use of a stylet, to intercept the 6th through 12th somatic nerves, on the transversus abdominis muscle. Contrasting data include narcotic usage, spirometrics, and arterial oxygen determinations before and after operations. Represented are 95 consecutive adult patients from the author's private practice done from 1971 to 1974. The anticipated postoperative hypoxemia and reduced pulmonary function of upper abdominal operations have been averted.

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Ingested metallic foreign body

Case Report

Anthony E. Loehr, MD and
G. B. DeBlanc, MD
Gallup, New Mexico

Pushing the pull-tab ring into the beverage can is common practice. This ring, if swallowed, is radiolucent.

The Otolaryngology Department of U.S. Public Health Service Indian Medical Center in Gallup, New Mexico, is confronted with a relatively large number of ingested foreign bodies on the Navajo, Zuni, and Hopi Indian Reservations. The following case report outlines diagnostic and therapeutic problems in the management of an ingested aluminum pull-tab ring top. This foreign object is relatively radiolucent, irregular, sharp, and non-magnetic. A brief review of esophageal and gastrointestinal foreign body problems is presented.

CASE REPORT

A 19-year-old Navajo female was admitted to the Gallup Indian Medical Center with throat and retrosternal pain in addition to dysphagia and odynophagia. Symptoms began four hours prior to admission, following the accidental ingestion of an aluminum pull-tab top ring from a beverage can. She had removed the pull-tab top ring and deposited the tab in the aluminum beer can. After accidentally ingesting the tab she noted immediate coughing with onset of the above symptoms. The patient denied any respiratory distress or hemoptysis. She was not intoxicated.

Past medical history was negative specifically for gastrointestinal or cardiopulmonary problems. Physical examination on admission was completely negative including indirect laryngoscopy. Chest (PA and lateral), soft tissue cervical and adbominal roentgenograms showed no evidence of abnormality or a foreign body.

Due to persistent symptoms in addition to the questionable radiolucency of the aluminum tab, it was decided to perform an endoscopic examination. In the operating room, an oral endotracheal general anesthetic was administered, and direct laryngoscopy and esophagoscopy were performed.

Endoscopic findings included mucosal abrasions of the posterior hypopharyngeal wall and the left arytenoid. Also, linear abrasions of the mucosa of the proximal esophagus were seen. Post-endoscopy, repeat chest, neck and abdominal x-rays did not disclose a foreign body.

The patient was observed in the hospital for two days with gradual resolution of symptoms. All stools were screened; however, no foreign body was recovered. There were no complications. The foreign body either tranversed the gastrointestinal tract or was regurgitated during initial coughing spells.

Comment

Numerous and bizarre nonedible ingested foreign bodies have been documented in the literature.[1-4] Metallic foreign bodies are usually easily localized by plain x ray films. Aluminum is relatively radiolucent depending on mass (thickness). Aluminum has a mass absorption of 0.169 cm2/gm at .10 Mev (Million electron volts).[5] A standard diagnostic x ray at the Indian Medical Center did not outline an aluminum tab lying flat in 12 centimeters of water.

Special radiographic procedures with contrast media can be used to localize non-opaque foreign bodies and/or pre-existing pathology. However, in an excellent review of esophageal foreign bodies, Tucker points out the dangers of contrast material.[6] If available, the modality of xeroradiology may be used to localize non-opaque foreign bodies. The relatively radiolucent foreign body represents a challenge in diagnosis, especially if a reliable history is unobtainable.[8]

Dr. Loehr is Chief Resident, Department of Otolaryngology, University of Colorado Medical Center, Denver. Dr. DeBlanc practices in Gallup, New Mexico. The opinions expressed in this paper are those of the author and do not necessarily reflect the views of the Indian Health Service.

Three additional cases of ingested aluminum tabs are reported in two recent brief communications.[9,10] The rather widespread use of aluminum beverage cans represents a problem of foreign body ingestion due to the ecologically inspired desire to prevent litter by placing pull-tab ring tops in the can immediately upon opening. These objects are irregular and sharp, thus the potential of esophageal or distal gastrointestinal perforation exists.[11,12] Ingested foreign bodies cause approximately 20 to 30 per cent significant esophageal problems. Perforations of the esophagus secondary to foreign bodies may result in life-threatening sequelae of T-E fistula, cervical abscess, mediastinitis, or pneumothorax.[14] Prompt diagnosis is important so that early correction of these problems can be initiated.[11,15] As reported by Stevenson et al, 75 per cent of ingested foreign bodies reach the stomach, and of this number 90 per cent will pass through the gastrointestinal tract without problems.[16,17]

Ingested objects that pass beyond the esophagus are generally treated by observation. During this conservative treatment, the size, nature and numbers of the foreign body are considered in addition to clinical signs, symptoms and radiographic progression.[13] A previous report from the Navajo Reservation presented management alternatives in straight pin ingestion in two Navajo children.[18]

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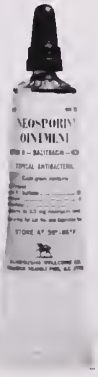

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Please include beneath the title or at the top of the first page a brief paragraph stating what the article is designed to show and, therefore, why it should be read. This introductory feature is, in editorial parlance, called the "blurb"; it is printed in bold type.

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7. Illustrations. A limited number of illustrations or "cuts," usually up to six, will ordinarily be accepted within our own publication budget if the editor believes they enhance the value of the article. Clear photos, simple diagrams or line drawings in black on white, printing rather than writing, reproduce well. Cuts should be mounted separately, and the paper or cardboard mounts should be the same size as that upon which the article is typed. Each should have its caption below: Fig. 1, Fig. 2, etc., with a short descriptive sentence. Authors will be billed our cost for excess above six cuts.

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12. Editorials. We would like to have more submitted by our State editors and the membership at large. Readers must get tired of thunder from publication headquarters in Denver; frankly, we do too! Speak out, and we'll sign your name, initials, or respect your request for anonymity, as you choose. If you don't like something we do or say, please let us in on it; we could even stand to hear about it if something happens to please you. A "Letter to the Editor" may help you get something off your mind. We're asking for it and we have a place to put it—in the Journal, that is!

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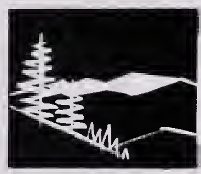


COLORADO

Grant Award for Fetal Diagnosis of Hemophilia

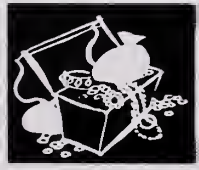
Marie-Louise Lubs, MD, assistant professor of pediatrics, University of Colorado School of Medicine, has been awarded a $2,000 grant for a six-month study for the National Foundation-March of Dimes. The purpose of the study is to determine whether amniocentesis, a prenatal test which discloses the presence of potential birth defects, might trigger a negative, clotting abnormality in a hemophiliac. Doctor Lubs will gather information from 41 medical centers where amniocentesis is carried out on a regular basis.

WYOMING

Patrick Elected to Office

Robert T. Patrick, MD, Casper, Wyoming, was reelected Vice President for Scientific Affairs of the American Society of Anesthesiologists at the annual meeting of the 13,500 member organization. A former president of the American Board of Anesthesiology, he has served with the Natrona County Memorial Hospital, Casper, as Secretary of the Medical Staff and Chairman, Department of Anesthesiology.

A native of Des Moines, Iowa, he attended Denison University, Granville, Ohio, and received the M. D. degree in 1944 from the University of Louisville School of Medicine. He later served as a staff member at the Mayo Clinic, Rochester, Minnesota, before moving to Casper. Doctor Patrick is a member of the Natrona County Medical Society, Wyoming State Medical Association, and the Wyoming State Board of Medical Examiners.



MONTANA

Tkach Scholarship Awarded

Oscar Bravo Yabar, a native of Cusco, Peru, has been named to receive a scholarship from The John R. Tkach, MD, Educational Trust, and will spend a year in high school in Bozeman, Montana. Travel and support costs are covered by the grant. In addition, Tkach Trustees were impressed by Pedro Klepper, adopted son of missionaries in the Urubamba River Valley, who seeks an educational opportunity to learn medicine, and bring needed medical care to the children of the Valley. For further information write: The John R. Tkach, MD, Educational Trust, Route 4, Box 60, Bozeman, Montana 59715.

MEDICAL SCHOOL NOTES

Eickhoff Named Acting Chairman

Theodore Eickhoff, MD professor of medicine and head of the Division of Infectious Disease, University of Colorado School of Medicine, has been named acting chairman of the CU Department of Medicine.

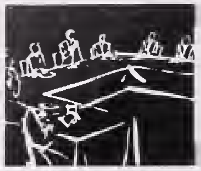
Dr. Eickhoff's appointment has been approved by the CU Board of Regents. He is succeeding Gordon Meiklejohn, MD, who retired after heading the department for 25 years.

Doctor Eickhoff, 44, received his MD degree from Western Reserve University School of Medicine, Cleveland, Ohio. After doing his internship and residencies at Boston (Mass.) City Hospital, he was a research fellow in medicine from 1962-64 at Harvard Medical School and Thorndike Memorial Laboratory, Boston City Hospital.

Following his fellowship, Dr. Eickhoff went to Atlanta, Ga., where he was clinical assistant professor of preventive medicine at Emory University School of Medicine, and deputy chief of the Investigations Section, Epidemiology Branch, Communicable Disease Center. In 1966, he became chief of the CDC Bacterial Diseases Section.

Dr. Eickhoff is the author or co-author of more than 70 articles, several of which deal with hospital-acquired infections. He is a consultant to the Bureau of Biologics, U.S. Food and Drug Administration, and a former consultant to the medical director of the National Aeronautics and Space Administration.

A fellow of the American College of Physicians, Dr. Eickhoff belongs to numerous organizations, including the American Federation for Clinical Research, American Society for Microbiology, American Hospital Association-Committee on Infections in Hospitals, American Board of Internal Medicine-Infectious Disease Subspecialty Committee and the FDA's Advisory Committee on Anti-Infective Drugs. He is a council member of both the American Society for Clinical Investigation and the Infectious Diseases Society.



MEETINGS

Foundation for Emergency Medical Education
National Seminar Program

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Brown Palace Hotel,
Denver, Colorado

November 14-16, 1975

Contact: Richard Rundell, National Seminar Program in Emergency Medicine, P.O. Box 014060, Flagler Station, Miami, Florida 33101.

The Children's Hospital

PEDIATRIC CRITICAL CARE

Brown Palace Hotel,
Denver, Colorado

November 21-22, 1975

Contact: Diane Terwelp, Department of Continuing Education, The Children's Hospital, Denver, Colorado.

American College of Physicians

NEW MEXICO REGIONAL MEETING

George Savage Auditorium,
Presbyterian Hospital Center,
Albuquerque, New Mexico

November 21-22, 1975

Contact: Fred H. Hanold, MD, 1421 Dartmouth, NE, Albuquerque, New Mexico 87106.

American Society for Surgery of the Hand

MICROSURGERY AND REPLANTATION

Brown Palace Hotel, Denver, Colorado
November 29-December 1-3, 1975

Contact: American Society for Surgery of the Hand, Three Parker Place, Suite 233, 2660 South Parker Road, Aurora, Colorado 80232.

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American College of Cardiology
Santa Barbara Heart and Lung Institute

FUTURE DIRECTIONS IN THE MANAGEMENT OF CARDIAC DISEASE— A BICENTENNIAL VIEWPOINT

Snowmass-at-Aspen, Aspen, Colorado

January 11-13, 1976

Contact: William D. Nelligan, American College of Cardiology, 9650 Rockville Pike, Bethesda, Maryland, 20014.

University of Oklahoma Department of Medicine—
National Academy of Medicine of Mexico

INTER-AMERICAN SYMPOSIUM OF INTERNAL MEDICINE

Centro Medico Nacional, Instituto Mexicano
Del Seguro Social, Mexico City, Mexico

January 12-15, 1976

Contact: James F. Hammarsten, MD, University of Oklahoma Health Sciences Center, P.O. Box 26901, Oklahoma City, Oklahoma 73190.

American College of Emergency Physicians-
Emergency Department Nurses Association

SECOND ANNUAL ROCKY MOUNTAIN REGIONAL CONFERENCE ON EMERGENCY MEDICINE AND NURSING

January 14-17, 1976

Keystone Lodge, Keystone, Colorado

Contact: Ellen H. Taliaferro, MD, St. Joseph Hospital, 1835 Franklin Street, Denver, Colorado 80218.

American College of Physicians

COLORADO REGIONAL MEETING

January 15-17, 1976

The Broadmoor, Colorado Springs, Colorado

Contact: Robert V. Elliott, MD, St. Luke's Hospital, 601 East 19th Avenue, Denver, Colorado 80203.

Albuquerque and Bernalillo County
Medical Association

VAIL MEDICAL-SKI SYMPOSIUM— CARDIOLOGY FOR THE NON-CARDIOLOGIST

January 16-17, 1976

Contact: David R. Holten, MD, 8401 Constitution, NE, Albuquerque, New Mexico 87110.

* * *

TAOS MEDICAL-SKI SYMPOSIUM

February 18-21, 1976

Contact: Thomas A. Bodnar, 2650 Yale Blvd., SE, Suite 103, Albuquerque, New Mexico 87106

* * *

PURGATORY MEDICAL-SKI SYMPOSIUM— HYPERTENSION 1976

Durango, Colorado

March 12-13, 1976

Contact: David R. Holten, MD, 8401 Constitution, NE, Albuquerque, New Mexico 87110.

Lovelace Foundation

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Contact: Martin J. Conway, MD, Lovelace Foundation, 5200 Gibson Blvd., SE, Albuquerque, New Mexico 87108.

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Recent Acquisitions

Cancer Chemotherapy: Martin J. Cline. 2nd ed. Philadelphia, Saunders, 1975. 324 p.

Cancer Chemotherapy: Clinical Conference on Cancer, M. D. Anderson Hospital and Tumor Institute. Chicago, Year Book, 1975. 577 p. $31.50.

Cardiac Catheterization and Angiography: William Grossman. Philadelphia, Lea and Febiger, 1974. 339 p. $22.05.

Diseases of Bones and Joints: Louis Lichtenstein. 2nd ed. St. Louis, Mosby, 1975. 314 p. $24.75.

Fundamentals of Family Practice: Wilfred Snodgrass. Philadelphia, Davis, 1975. 634 p. $35.00.

Hand-Atlas of Human Anatomy: Werner Spalteholz. 7th ed. Philadelphia, Lippincott. 902 p. Gift.

The Nature and Treatment of Depression: Frederic F. Flach. New York, John Wiley and Sons, 1975. 422 p. $19.75.

Novak's Textbook of Gynecology: Edmund R. Novak. 9th ed. Baltimore, Williams and Wilkins, 1975. 822 p. $25.65.

Personality Disorders: John R. Lion. Baltimore, Williams and Wilkins, 1974. 432 p. $18.90.

Progress in Gynecology: Melvin L. Taymor and Thomas H. Green Jr., eds. New York, Grune and Stratton, 1975. v. 6. 782 p. $41.50.

Respiratory Insufficiency: Benjamin Burrows. Chicago, Year Book, 1975. 187 p. $9.50.

Synopsis of Gynecologic Oncology: Philip J. Disaia. New York, John Wiley and Sons, 1975. 344 p. $19.50.

Synopsis of Ophthalmology: William H. Havener. 4th ed. St. Louis, Mosby, 1975. 594 p. $13.05.

Understanding Aging: A Multidisciplinary Approach: Marian Spencer and Caroline J. Don, eds. New York, Appleton-Century, 1975. 286 p. $11.25.

Are you aware of the copyright crisis? The Committee on Legislation in the House of Representatives is considering a revision of the copyright law which would prohibit libraries from photocopying, especially for interlibrary loan. If HB 2223 is passed with Section 108G2 intact, any librarian who photocopies copyrighted material is liable to a fine of up to $50,000. The library will be happy to supply the names and addresses of committee members to anyone interested in contacting same.

Biological Psychiatry, edited by Joseph Mendels, with 25 contributors, bibliographies, 512 pages, $27.50, John Wiley & Sons, N.Y., 1972.

Says Dr. Mendels at the end of his very brief preface, "Whatever the ultimate source of psychiatric illness, it is reasonable to anticipate that it will be expressed through the brain, with inputs from the autonomic nervous system, and the neuroendocrine complex. More complete understanding of these intersections is therefore crucial. This book is directed toward that goal."

It is refreshing and reassuring to see a thoroughgoing effort to approach psychiatric illness from the organic standpoint. This is not to deny the great importance of situational and environmental influences, yet, as Dr. Mendels says, these will be received and stored and expressed organically.

I think that most physicians will consider this book "hard reading", and the respective bibliographies are truly formidable. However, it is a most reassuring production, and every member of the healing professions will find it an inspiration.

Horace E. Campbell, M.D.
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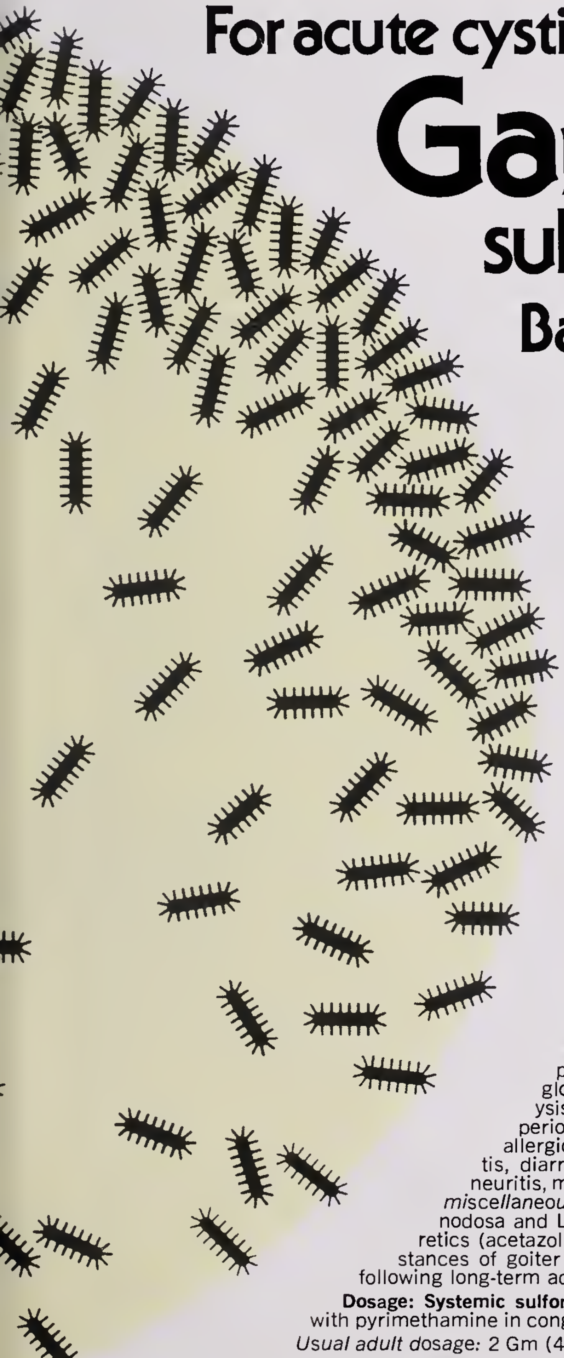

For acute cystitis*

Gantanol® B.I.D.
sulfamethoxazole/Roche®

Basic therapy with convenience:
4 tablets (0.5 Gm each) STAT — then 2 tablets B.I.D. for 10 to 14 days

*Nonobstructed; due to susceptible strains of *E. coli*

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Acute, recurrent or chronic nonobstructed urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms. ***Note:* Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections.** Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

Contraindications: Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

Warnings: Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

Precautions: Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

Adverse Reactions: *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age (except adjunctively with pyrimethamine in congenital toxoplasmosis).

Usual adult dosage: 2 Gm (4 tabs or teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

Usual child's dosage: 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

Supplied: Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

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Division of Hoffmann-La Roche Inc.
Nutley, New Jersey 07110

in Brief

A summary of AMA, medical & health news

American Medical Association / 535 North Dearborn Street / Chicago, Illinois 60610 / Phone (312) 751-6000 / TWX 910-221-0300

Incorporation of an AMA professional liability reinsurance company was recently authorized by the Board of Trustees. The facility will be known as the American Medical Assurance Co. Before the company can become operational, $1 million in capital and $1 million in surplus will be required as funding, and arrangements must be completed with state medical societies participating in the program. The purpose of the AMA company will be to provide increased capacity, added capital, and technical assistance to local society insurers writing primary professional liability insurance directly to physicians.

An Idaho trial court declared that setting maximum limits on physicians' liability is unconstitutional. After passage of the state's professional liability law containing maximum limits, the Idaho Medical Assn. sought an advisory decision by the state's Supreme Court on the constitutionality of the provision. The request was rejected. In a case before the trial court, the maximum limit provision was declared unconstitutional. The case will now be appealed to the Idaho Supreme Court.

HEW's official notice withdrawing utilization review regulations for Medicare and Medicaid because of the AMA's successful suit for a preliminary injunction was published in the Sept. 10 *Federal Register*. The regulations are being rewritten and will be republished for comment. After HEW announced it would make changes in the regulations, the AMA dismissed its suit, filed Feb. 20, without prejudice, meaning that it can be filed at a later date if necessary.

The week of April 4 has been designated National Rural Health Week, as part of the nation's Bicentennial. Sponsored by the AMA in conjunction with the American Dental Assn., American Hospital Assn., American Veterinary Medical Assn., U.S. Depts. of Agriculture and HEW, and the National Safety Council, the week will coincide with the 29th National Conference on Rural Health in Phoenix, April 8-9, 1976. In December, the AMA will mail National Rural Health Week Community Action Kits to state and non-metropolitan county medical societies.

The Comprehensive Health Insurance Act of 1975, the AMA's new NHI plan, is outlined in a booklet--"A National Health Insurance Plan Designed by America's Physicians." Copies have been sent to presidents and executive directors of state, metropolitan county and specialty medical societies.

Mark your calendars for two important 1976 AMA meetings. The 1976 AMA National Leadership Conference will be Jan. 22-25 at the Marriott Motor Hotel, Chicago, and the Public Affairs Workshop will be April 10-12 at the Shoreham Hotel in Washington, D.C.

A "Special AMA News Bulletin," the second of its kind this year, mailed to all U.S. physicians, noted that more than 54% of the AMA's budget is spent to improve the delivery of medical and health care. Only about one-half of one percent is allocated to the Dept. of Congressional Relations, or lobbyist activity, the bulletin said.

State medical societies wishing to conduct training programs for physicians interested in becoming medical directors of skilled nursing facilities may receive financial and technical assistance from the AMA. The assistance is made possible through the extension of an AMA-HEW contract. A federal requirement that all skilled nursing facilities have a medical director becomes effective Jan. 1, 1976. State societies interested in conducting seminars should contact Dept. of Hospitals and Health Facilities, AMA Headquarters.

Available from AMA: "Action Guide for Maternal and Child Care Committees" provides a step-by-step approach to discover and attack maternal and child care problems in a state or a community. OP-439 is available for $1 per copy; 90¢ for 11-49 copies, and 80¢ for 50 or more from Order Dept., AMA Headquarters...A comparison of major national health insurance proposals, prepared by the AMA's Legislative Dept. as a special Aug. 29 edition of *Legislative Roundup*, is available in limited quantities from the department.

OBITUARIES

Colorado

Theodore E. Beyer, MD, died Monday, July 28, 1975 in the Valley Hi Nursing Home, Denver at the age of 91. He was born in Milwaukee, Wisconsin on June 26, 1884. Following a brush with the tubercle bacillus at age 17 years, he spent several months with relatives in South Dakota. After regaining his health, he attended Yankton College in South Dakota, receiving his BA in 1908.

After teaching school for a few years, he attended the University of Wisconsin, receiving a Master's degree in toxicology in 1913. He then entered Rush Medical College in Chicago, graduating with his MD degree in 1915. Towards the end of his two year internship at Cook County Hospital in Chicago, he experienced reactivation of his old lung trouble which resulted in his coming to Denver to "chase the cure".

After two years in Agnes (Phipps) Memorial Sanitorium as part-time patient and part-time physician, he opened an office in Denver for the practice of medicine and otolaryngology. He acquired the positions of industrial surgeon for the Union Pacific Railroad, the Denver Tramway Company, and the American Smelting and Refining Company.

Over the years he became increasingly involved with otolaryngology, ultimately limiting his practice to that discipline. He was one of Denver's first endoscopists, and contributed substantially to the medical literature in the fields of otolaryngology and endoscopy.

Doctor Beyers was certified by the American Board of Otolaryngology in 1925. He was a member of the Denver and Colorado Medical societies, and the American Medical Association. He was a Fellow of the American College of Surgeons, and a member of the Colorado Otolaryngological Society, the American Academy of Otolaryngology, and the Denver Clinical and Pathological Societies. He was a member of the Mercy Hospital Medical Staff.

He served as president of the Denver Medical Society, the Colorado Otolaryngological Society, the Denver Clinical and Pathological Society, and the Mercy Hospital Medical Staff. He was a member of the Credentials Committee of the American College of Surgeons.

In 1960 he retired from active practice, and resided for a while in La Jolla, California.

In 1914 he was married to Margaret Metcalfe of Council Bluffs, Iowa. She died in 1947. In 1948 he was married to Mrs. Mabel Blair, the mother of his associate in medical practice, James R. Blair, MD. His second wife died in 1954. In 1960 he was married to Mrs. Charlotte Hoffman of West Englewood, New Jersey, who survives the doctor, as does a daughter, Ann, wife of Dr. Robert J. Wert, president of Mills College, Oakland, California.

George Balajty, MD, died July 16, 1975 in St. Joseph Hospital, Denver, after a prolonged illness. He was 74 years of age, having been born in Hungary in 1900.

He received his medical education at the University of Hungary in Budapest, then took his graduate training at the University of Vienna in Austria. His specialty was internal medicine, and cardiology. He came to the United States in 1947, and held a faculty appointment at the University of Colorado School of Medicine. He opened an office for general practice in Denver about 1949.

He was a member of the Denver and Colorado Medical societies, and of the American Medical Association. He was a staff member of St. Joseph and St. Luke's hospitals. He belonged to the Cherry Hills and Pinehurst Country clubs.

His first wife Maya Perenyi Balajty died in 1962. He is survived by Mrs. Jean Balajty, whom he married in 1969, and by a daughter, Mrs. H. L. Ambrose of Denver, and by two grandsons.

Casper Markel, MD, died Tuesday, September 23, 1975 at the age of 79 years in Beth Israel Hospital, Denver. Born September 1, 1896 in Annandale, New Jersey, he took his premedical work and later medical studies at the University of Colorado, receiving his degree in 1920.

After an internship served at the Harper Hospital, Detroit, Michigan, and at the Bronx Hospital, New York City, he served a residency in Diseases of the Chest at the Jewish Consumptive Relief Society Hospital near Denver.

He practiced Internal Medicine and Diseases of the Chest in Denver for nearly 50 years.

Doctor Markel was certified by the American Board of Internal Medicine and held the academic rank of Assistant Clinical Professor of Medicine at the University of Colorado School of Medicine. He was a member of the Denver and Colorado Medical societies and of the American Medical Association. He was a Fellow of the American College of Physicians, the American College of Chest Physicians, and the Association of American Medical Colleges. He was a member of the American Heart Association and the Sigma Xi Scientific Fraternity.

During his active years he was a consulting physician to the staff at the J.C.R.S. Hospital, an attending physician at Denver General Hospital, and an out-patient physician at the University of Colorado Medical Center. He was on the Active Staffs of Beth Israel and Rose Memorial Hospitals. He was an examining physician for Selective Service during World War II.

Doctor Markel has no known surviving relatives.

WANT ADS

MEDICAL OFFICE SPACE AVAILABLE in Professional Arts Building, 1245 East Colfax Avenue, Denver, located close to Midtown Hospital Area. Predominantly medical building at attractive rates. Contact: Mr. E. Crust, Richter/Robb & Co., (303) 831-7888. 674-8-TFB

PHYSICIAN WANTED. Man or woman. If you are looking for a change in your life style, then collaborate with a Ph.D. Molecular Biologist in research or Medical Services. Long-term association contemplated. Phone evenings and weekends collect, between 8 p.m. and 11 p.m.: (212) 675-7398 or Write: Ronald Friedman, Ph.D., P.O. Box 261, Bronx, New York 10463. 775-5-6B

INTERNIST NEEDED for active 96-bed GM&S Veterans Administration Hospital, well-equipped and staffed, with excellent library and consultants. Must be Board-qualified with solid medical background. Salary: $30-36,000; excellent fringe benefits; will pay travel and moving expenses; housing on hospital grounds. Equal opportunity employer; licensure required in one of the fifty states or District of Columbia. Abundant outdoor recreation; pleasant climate with clean air in attractive peaceful western city of 10,000. Inquire: Norman C. Jorgenson, MD, Chief of Staff, or T. L. Massey, Hospital Director, VA Hospital, Miles City, Montana 59301, or call collect: (406) 232-3060. 975-6-4B

PHYSICIAN'S ASSISTANT, AMA approved Class A School graduate, M.S. in physiology, wishes to locate in small mountain community. Excellent references. Reply Werner Studer, 709 Drury Lane, Wichita, Kansas 67207, or Phone: (316) 684-7549. 1075-1-2B

WANTED: OB-GYN and General Surgeon, Board certified or eligible, for university town in Southwestern New Mexico mining community, in seven man multispecialty group. Prefer American graduate. Write: Raymond T. Smith, Clinic Manager, Med Square Clinic, 114 West 11th Street, Silver City, New Mexico 88061. 1075-4-3B

UROLOGIST, 29, completing top university residency July 1976, seeks solo, group, or partnership. All situations considered. Write: Box 1075-7-2B, Rocky Mountain Medical Journal, 1601 East 19th Avenue, Denver, Colorado 80218. 1075-7-2B

ROCKY MOUNTAIN CONFERENCE ON MENTAL HEALTH, Vail, Colorado, March 13-20. 1976 Topic: Assignment of Treatment Careers. For information write Universal Travel, 3113 East Third Avenue, Denver, Colorado 80206. 975-2-2B

GRAND JUNCTION—FOR RENT or LEASE: Offices in high-ranking location near St. Mary's Hospital, X-ray and laboratory adjacent. Call: (303) 243-0726 or write: H. R. Bull, MD, Suite 10, 2232 North 7th, Grand Junction, Colorado 81501. 1175-1-3B

CERTIFIED PHYSICIAN'S ASSISTANT desires employment with physician (Family Practice preferred) Colorado area of choice—other states considered. References and resume upon request. Write: Lance Lewandowski, 1724 Ashley Hall Road, Apt. M, Charleston, South Carolina 29407. 1175-3-3B

COLORADO GENERAL PRACTITIONERS, GENERAL SURGEONS, ORTHOPEDISTS interested in rural community. 30-bed hospital-accredited. Office space and financial assistance available. Growing and healthy economic area, serving 12,000. Ski Country USA. All outdoor sports readily accessible. Write: Harvey Hartzler, Administrator, Memorial Hospital, 780 Tucker, Craig, Colorado 81625 or call: (303) 824-6578. 1175-4-3B

PHYSICIAN WANTED. Family physician or internist as medical director for an established medical program in a clean industrial organization. Excellent fringe benefits, including liability insurance, and pleasant working conditions in a choice college town of 50,000. For further details write or call: Medical Department, Woodward Governor Company, P.O. Box 1519, Fort Collins, Colorado 80522 or call: (303) 482-5811. 975-9-3B

POSITIONS AVAILABLE for Board Certified/Eligible General Internists for addition to multi-specialty group beginning November 1975. Additional position open for Internist/Gastroenterologist in January 1976. Contact: Colorado Permanente Medical Group, Suite 706, 2045 Franklin Street, Denver, Colorado 80205. 975-10-3

WANTED: Used equipment for family practice, including examining table. Call: Peter Monheit, MD. (303) 771-1647. 975-11-3

POSITIONS AVAILABLE FOR PSYCHIATRISTS, adult and child, full time, for growing Colorado HMO beginning 1976. Emphasis on eclectic, brief, and group therapy. Salary negotiable. No private practice allowed. Good fringe benefits. Contact: W. L. Reimers, MD, 2045 Franklin Street, Denver, Colorado 80205. 975-12-4

FOR SALE: 1 Sanborn EKG. 1 Diathermy-Challenger, Birtcher Model 850. 1 Birtcher Megason VI, Birtcher Model 106-5. 1 Leitz Photrometer. Call Mrs. George Balajty at (303) 832-1590, or write Mrs. George Balajty, 800 Lafayette Street, Denver, Colorado 80218. 975-14-TFB

VAIL, COLORADO OPENING for General Practitioner or Family Practitioner with an interest in Trauma and Orthopedics. Join a Family Practitioner for the 1975-76 ski season, with an opportunity for a permanent position. For details write G. R. Dooher, MD, Box 2086, Vail, Colorado 81657, or call: (303) 476-2129 after 7 p.m. 975-13-3

PHYSICIAN'S ASSISTANT, AMA approved Class A school graduate, M.S. in physiology, wishes to locate in small mountain community. Excellent references. Reply: Werner Studer, 709 Drury Lane, Wichita, Kansas 67207, or Phone: (303) 684-7549. 1075-1-2B

FAMILY PRACTITIONER—BRAND NEW FACILITY located 20 minutes from ski area, and 25 minutes from Denver. Salary negotiable. Contact: G. E. Cimochowski, MD, P.O. Box 1856, Evergreen, Colorado 80439 or call: (303) 674-7694. 1175-5-2

EMERGENCY MEDICINE PHYSICIANS: Highly remunerative situations available for EM physicians licensed or eligible for license in Texas, Oklahoma, New Mexico, or Louisiana. Major metropolitan medical centers, suburban and rural hospitals, and community practices throughout the Southwest. Excellent earnings and guarantees. For personalized confidential service at absolutely NO FEE to the candidate, send CV to Toni Clark, Search Committee, Daniel Stern and Associates, Health Placement Services, Suite 510 GPM South Tower, 800 NW Loop 410, San Antonio, Texas 78216. 1175-7-2B

PERFECT! For the professional who wants a professionally decorated and furnished condominium located in Strawberry I on the 11th green, with a spacious view of city and mountains. Flirts with everything but your pocket book. For a personal showing call: Harold Arnold, (303) 794-0918 or 795-8122. Century 21. Stark Realty. 1175-8-1B

WIT, IRREVERENCE, AND EXCELLENCE are the marks of nine original signed etchings in portfolio by the noted artist Charles Bragg, entitled Major Medical. Perfect for the physician's den or office. Contact: N. A. Bragg, 65 Benthaven Court, Boulder, Colorado 80303 or call: (303) 837-2771 (O) or 499-3259 (H). 1175-9-1B

PHYSICIANS ASSOCIATE—Family Practice. Duke University graduate 1973 wants to relocate in Denver area. For further information write: Mr. James Ellis, 1401 Golf Road, Waukegan, Illinois 60085. 1175-2-3B

NEEDED: GENERAL AND THORACIC SURGEON to join Surgical Department of Great Falls Clinic, a 28-doctor multispecialty group. Contact: Administrator, Great Falls, Clinic, 1220 Central Avenue, Great Falls, Montana 59403. 1175-10-2B

WANTED: INTERNIST with cardiology subspecialty, to join three internists in medical department of multispecialty clinic in Western Montana. Unexcelled opportunities for outdoor recreation. New clinic building, corporate structure with pension and profit-sharing plan. Write: Box 1175-11-3, Rocky Mountain Medical Journal, 1601 E. 19th Ave., Denver, Colorado 80218. 1175-11-3

ANESTHESIOLOGIST—This hospital is recruiting for highly qualified experienced anesthesiologist to work on a full-time or part-time basis. 439-bed hospital is fully integrated with the Medical School of the University of Colorado under postgraduate training. Co-appointment with the University possible. Excellent fringe benefits. Salary commensurate with education and experience. An equal opportunity employer. Contact: Roger Mitchell, MD, Chief of Staff, Veterans Administration Hospital, 1055 Clermont Street, Denver, Colorado, 80220 or call: (303) 399-8020, extension 401. 1175-12-1B

PHYSICIAN'S ASSISTANT seeking position within a clinical practice. Have eleven years experience in all realms of medicine. If you are considering a Physician's Assistant, please call for a resume and interview at (303) 287-9536; or write Joseph E. Bigley, 9240 Gaylord Street, Thornton, Colorado 80229. 1175-13-1B

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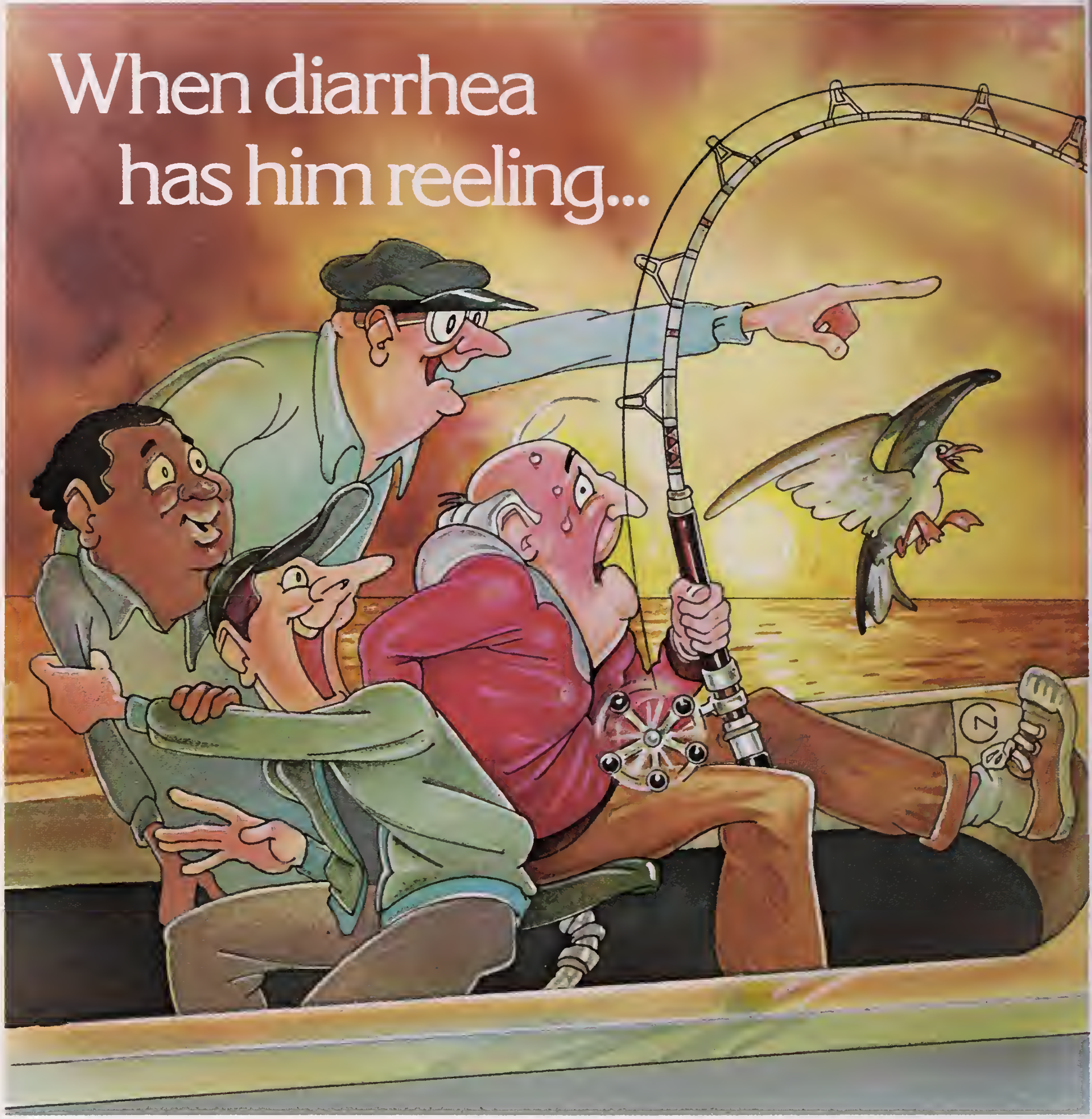
When diarrhea has him reeling...

Diarrhea can hook anyone. When it does, physicians and patients both want prompt control of diarrheal symptoms. Lomotil will usually control diarrhea promptly.

This rapid action can halt the emergency aspect of diarrhea and is comforting and reassuring to the patient. Electrolyte and fluid losses can be corrected while the specific cause of the diarrhea is being determined. If an infective agent is the cause, appropriate specific therapy should be given along with Lomotil.

Lomotil is contraindicated in children less than 2 years old.

Lomotil® TABLETS LIQUID

Each tablet and each 5 ml of liquid contain diphenoxylate hydrochloride 2.5 mg (Warning: May be habit forming), atropine sulfate 0.025 mg

holds the line.

IMPORTANT INFORMATION: *This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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San Juan, Puerto Rico 00936

Address medical inquiries to:
G. D. Searle & Co.
Medical Department, Box 5110,
Chicago, Illinois 60680

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Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration

The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

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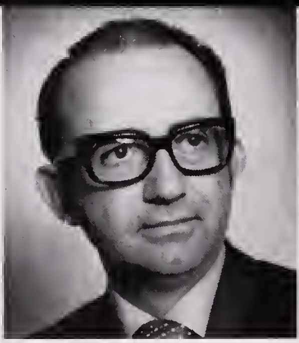

Dr. James H. Sammons
Executive Vice President
of the American
Medical Association

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socioeconomic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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Ecclesiastes 11:7

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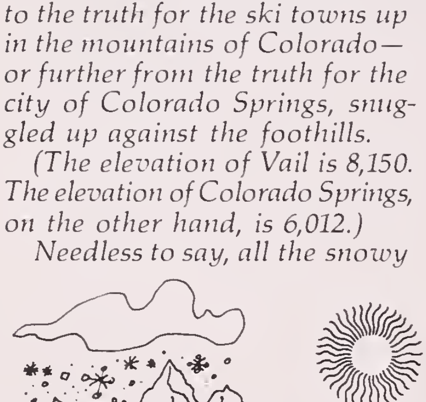
(The elevation of Vail is 8,150. The elevation of Colorado Springs, on the other hand, is 6,012.)

Needless to say, all the snowy publicity Colorado's ski areas have gotten has had an unfortunate effect on the winter business at Colorado's premier year-'round resort.

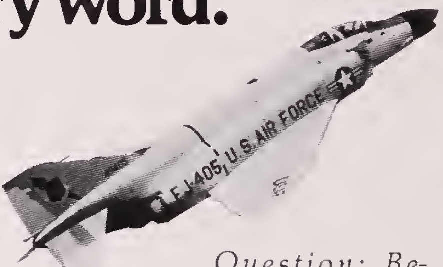


Them. Us.

(In a moment, we'll show how those of you planning a winter convention can take advantage of this situation.)

Question: Do you think the United States Air Force could have chosen Vail or Aspen as the site for the Air Force Academy?

Answer: No. They wanted a place with good flying weather all year 'round for the cadets to train in. (This probably explains why the Academy isn't a lot of other places, too. Like Cincinnati, Milwaukee, Philadelphia, or Minneapolis.)



Question: Between rounds at the World Figure Skating Championship (held in The BroAdmoor Ice Arena), do the athletes unwind by swimming in our outdoor pool? In February?

Answer: Yes.

Enough on the weather. Now let's talk about whether it's easy to get to The BroAdmoor in the winter. Once again, the answer is yes. (In more ways than one.)

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Of course, just being at The BroAdmoor makes any room special. Where else can you find all this: A lake, indoor tennis courts, a huge International Center (perfect for big meetings), an indoor ice skating rink, a movie theater, and a zoo? Plus The BroAdmoor shops (like Abercrombie & Fitch) and restaurants (like the fabulous Penrose Room) and taverns (like The Golden Bee, an authentic pub we brought over—intact—from England).

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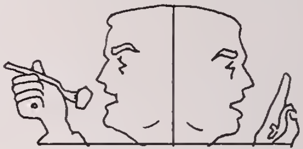

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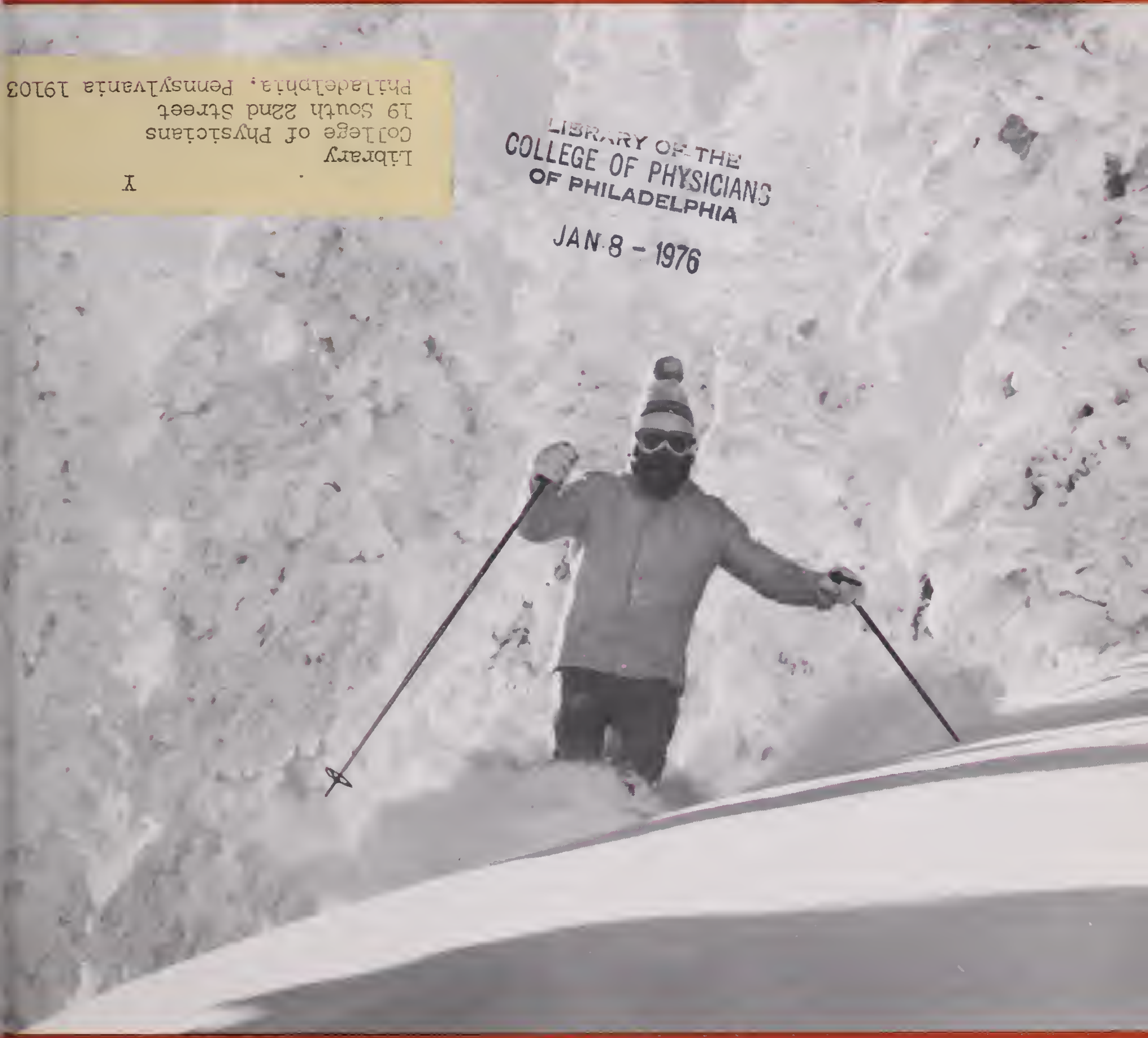

Season's Greetings

Both often

Predominant psychoneurotic anxiety
Associated depressive symptoms

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders, athetosis, stiff-man syndrome, convulsive disorders (not for sole therapy).

Contraindicated: Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

Warnings: Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequenc and/or severity of grand mal seizures ma require increased dosage of standard anti convulsant medication; abrupt withdrawa may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and mus cle cramps, vomiting and sweating). Keep addiction-prone individuals under careful

respond to one

According to her major
ymptoms, she is a psychoneu-
otic patient with severe
nxiety. But according to the
escription she gives of her
eelings, part of the problem
nay sound like depression.
This is because her problem,
lthough primarily one of ex-
essive anxiety, is often accom-
anied by depressive symptom-
tology. Valium (diazepam)
an provide relief for both—as
he excessive anxiety is re-
ieved, the depressive symp-
oms associated with it are also
ften relieved.

There are other advan-
ages in using Valium for the
nanagement of psychoneu-
otic anxiety with secondary
lepressive symptoms: the
sychotherapeutic effect of
Valium is pronounced and
apid. This means that im-
provement is usually apparent
in the patient within a few days rather than in a week or two, although it may take longer in some patients. In addition, Valium (diazepam) is generally well tolerated; as with most CNS-acting agents, caution patients against hazardous occupations requiring complete mental alertness.

Also, because the psychoneurotic patient's symptoms are often intensified at bedtime, Valium can offer an additional benefit. An *h.s.* dose added to the *b.i.d.* or *t.i.d.* treatment regimen can relieve the excessive anxiety and associated depressive symptoms and thus encourage a more restful night's sleep.

Valium® (diazepam) Ⓘⓥ

2-mg, 5-mg, 10-mg scored tablets

in psychoneurotic
anxiety states
with associated
depressive symptoms

urveillance because of their predisposi-
ion to habituation and dependence. In
pregnancy, lactation or women of child-
earing age, weigh potential benefit
gainst possible hazard.

recautions: If combined with other psy-
hotropics or anticonvulsants, consider
arefully pharmacology of agents em-
loyed; drugs such as phenothiazines,
arcotics, barbiturates, MAO inhibitors
nd other antidepressants may potentiate
ts action. Usual precautions indicated in
atients severely depressed, or with latent
lepression, or with suicidal tendencies.
Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

Side Effects: Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Before prescribing, see complete prescribing information in SK&F literature or *PDR*. The following is a brief summary.

* **Warning**
This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

***Indications:** *Edema:* That associated with congestive heart failure, cirrhosis of the liver, the nephrotic syndrome; steroid-induced and idiopathic edema; edema resistant to other diuretic therapy. *Mild to moderate hypertension:* Usefulness of the triamterene component is limited to its potassium-sparing effect.

Contraindications: Pre-existing elevated serum potassium. Hypersensitivity to either component. Continued use in progressive renal or hepatic dysfunction or developing hyperkalemia.

Warnings: Do not use dietary potassium supplements or potassium salts unless hypokalemia develops or dietary potassium intake is markedly impaired. Enteric-coated potassium salts may cause small bowel stenosis with or without ulceration. Hyperkalemia (>5.4 mEq/L) has been reported in 4% of patients under 60 years, in 12% of patients over 60 years, and in less than 8% of patients overall. Rarely, cases have been associated with cardiac irregularities. Accordingly, **check serum potassium during therapy, particularly in patients with suspected or confirmed renal insufficiency (e.g., elderly or diabetics). If hyperkalemia develops, substitute a thiazide alone. If spironolactone is used concomitantly with 'Dyazide', check serum potassium frequently**—both can cause potassium retention and sometimes hyperkalemia. Two deaths have been reported in patients on such combined therapy (in one, recommended dosage was exceeded; in the other, serum electrolytes were not properly monitored). Observe patients on 'Dyazide' regularly for possible blood dyscrasias, liver damage or other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium (triamterene, SK&F). Rarely, leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with the thiazides. Watch for signs of impending coma in acutely ill cirrhotics. Thiazides are reported to cross the placental barrier and appear in breast milk. This may result in fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and possibly other adverse reactions that have occurred in the adult. When used during pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus.

Precautions: Do periodic serum electrolyte and BUN determinations. Do periodic hematologic studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in postsympathectomy patients. The following may occur: hyperuricemia and gout, reversible nitrogen retention, decreasing alkali reserve with possible metabolic acidosis, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), digitalis intoxication (in hypokalemia). Use cautiously in surgical patients. Concomitant use with antihypertensive agents may result in an additive hypotensive effect. 'Dyazide' interferes with fluorescent measurement of quinidine.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting (may indicate electrolyte imbalance), diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

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Spiritual support in patient care

In its continuing program to promote better total care for patients, in 1961 the American Medical Association formed its Department of Medicine and Religion. This effort encouraging a close clergy-physician relationship is recognition that the spiritual needs of the sick should not be neglected. Commenting on the team effort in medical care, Dr. J.E. Holoubek said, "The patient's clergyman is an invaluable asset. In times of crisis, he is often the first person called by the family; he should be capable of determining which conditions he can handle in spiritual counseling and which require the assistance of a physician."[1] It should be added, that for patients already under medical care, it is equally important that the physician recognize the patient's need for a spiritual counselor, and when required, help arrange for this consultation. What this means in its practical application is the burden of this review.

Soren Kierkegaard, the Danish philosopher and theologian, said, "Affliction is able to drown out every earthly voice . . . but the voice of eternity within a man it cannot drown."[2] Those who accept the truth of this observation will realize that it must be dealt with in the practice of medicine. Perhaps Robert Louis Stevenson, who died of tuberculosis in 1894, exemplifies as well as any other the challenge of a serious illness and what spiritual help can mean to such a patient. In conversation with an old friend, Will Low, he is reported to have said, "Low, I wish to live! Life is better than art, to do things is better than to imagine them, yes, or to describe them. And God knows, I have not lived all these last years. No one knows, no one can know, the tedium of it. I've supported it as I could—I don't think that I am apt to whimper—but to be, even as I am now, is not to live."[3] His reliance on divine help in facing the ravages of disease is well documented in his prayers.[3] Through faith, Stevenson found the strength to endure and to lead a productive life in spite of being seriously disabled most of his adult life. He was only forty-four when he died, but his contributions to English literature are forever.

In a more recent documentation of a patient's feeling during a crisis, the press quoted Stuart Alsop, the famous American author, as stating three months before his death from leukemia in June 1974: "I remember waking up about four in the morning and having a feeling that I've never had before . . . a kind of a ghastly loneliness . . . a feeling that I'd never see another Spring . . . a sudden total despair came over me"[4]—a dramatic expression of what many physicians hear in more simple terms from seriously ill or terminal patients.

Ill health can try man's soul. It is appropriate, therefore, that physicians, nurses, and others providing professional medical help for patients, recognize the additional responsibility imposed. Addressing this viewpoint, Dr. Robert B. Greenblatt wrote, "The physician cannot study man in the biologic sense alone, for man's soul must be so nurtured that his body may function harmoniously in all its parts."[5] To accomplish this end, all conditions which affect or influence the needs of the body (physical strength), the mind (emotions, intellect and will), and the soul (spiritual strength), must be evaluated.

It has long been known that seriously ill patients who have a chance for recovery, improve that chance if they have faith. While the latter has many components, certainly the most important are faith in human help—the skill of medical science and the support of family and loved ones, faith in Divine help—the source of spiritual strength, and finally, faith in self and the ability to endure the trial. As testimony to the importance of religious faith in the recovery from a serious emotional illness, Carl Gustav

Jung (1875-1961), the famous Swiss psychologist said, “Man has always stood in need of the spiritual help which each individual’s own religion held out to him . . . Among all my patients in the second half of life—that is to say, over thirty-five—there has not been one whose problem in the last resort was not that of finding a religious outlook on life. It is safe to say that everyone of them fell ill because he had lost that which the living religions of every age have given to their followers, and none of them has been really healed who did not regain his religious outlook.”[6]

With these observations in mind, it is reasonable to conclude that physicians do have a responsibility to evaluate the needs of seriously ill or distraught patients from the standpoint of body, mind, and soul. They should know, of course, the patient’s religious background and, if receptive, suggest that a clergyman of the patient’s faith provide spiritual counseling. Lending moral support to ministerial services when needed, is recognition that this help is an integral part of patient care. For those who might be hesitant or self-conscious about becoming personally involved in facilitating this service, the eminent educator and former president of Harvard, Nathan M. Pusey, offers these thoughtful words of encouragement: “It would seem to me that the finest fruit of serious learning should be the ability to speak the word of God without reserve or embarrassment, certainly without adolescent resentment; rather with some sense of communion, with reverence and with joy.”[8]

The favorable influence of spiritual strength during some trial in life—including that of ill health—has long been recognized and accepted by fair minded observers. Leaders in the health professions are usually mindful of this when planning for patient services and particularly when considering those who fall in the serious or terminal category. “Man’s nature, and therefore, his illnesses, have mental, physical, and spiritual components. A wise physician will recognize that his patient, in his total being, requires the assistance of all available to help him.”[1] Spiritual support is an important part of total patient care, and our clergy members of the “health team” should receive the cooperation needed to make this possible. Physicians and other members of the healing arts who participate in this aspect of patient care have an opportunity of making the applications of their own personal faith a more meaningful and rewarding experience.

Carl W. Tempel, MD, Denver*

ACKNOWLEDGEMENT. Review of this manuscript and recommendation by Chaplain (Colonel) Robert E. Johnson, Chief Chaplain, Fitzsimons General Hospital, Denver, is gratefully acknowledged.

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* Dr. Tempel is former Chief of Medicine and Commander, Fitzsimons General Hospital, Denver, Clinical Professor of Medicine, Emeritus, University of Colorado Medical Center, and Consultant in Tuberculosis Control, Colorado Department of Health.

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OUR COVER

Skiing in a winter wonderland, amidst a miracle of snowy, frosted trees, this skier is experiencing that incomparable feeling of entering where no other has been—since the snow fell. Up there no man is alone. Credit: Colorado Ski Country USA.

Effects of altitude in persons with sickle hemoglobinopathies*

J.H. Githens, MD, C. R. Phillips, MD, J. R. Humbert, MD, S.E. Bonner, RN, P.C. Ewing, MD, Denver & Boulder, Colorado

Reviews of the literature and experience of the Colorado Sickle Cell Center on the effects of altitude in persons with sickle hemoglobinopathies indicate that the "sudden death syndrome" is not caused by altitude or sickle cell trait. However, splenic sequestration crises do occur at high altitude and persons with sickle/hemoglobin C disease are especially at risk.

PREVIOUS REPORTS in the medical literature have suggested that persons with sickle cell trait who are exposed to altitude may develop splenic and pulmonary infarcts[1] or even be more susceptible to sudden death from extreme exertion.[2] Persons with other sickle hemoglobinopathies are also believed to be at greater risk of developing crises at high altitude.

We have recently surveyed the literature and our own experience in an attempt to evaluate the risk of possible health problems in persons with sickle hemoglobin who are exposed to high altitude.

"Sudden Death Sydrome"

During the fall of 1974 interest and concern developed in the Rocky Mountain area regarding the possible relationship between sickle cell trait, altitude, exertion, and sudden death. This interest was triggered by the sudden, unexpected death of a black athlete in Boulder, Colorado, who was found to have sickle cell trait. The course of his brief illness was characterized by the acute onset (during exercise) of severe pain in the leg muscles and collapse, followed by renal insufficiency, acidosis, disseminated intra-vascular coagulation, cardiac arrest, and death. The autopsy revealed primarily renal and hepatic necrosis with severe plugging of vessels with sickled cells, particularly in the kidney and the liver.[3] The clinical picture was very similar to that reported by Jones et al under the title "Sudden Death in Sickle Cell Trait"[2] which described four black recruits who developed this syndrome while undergoing army training at an altitude of of 4,060 feet. In all four cases sickling was found at autopsy and in three of the four the hemoglobinopathy was identified as sickle cell trait.

Since the degree of hypoxia that occurs with death is sufficient to cause sickling in persons with sickle cell trait, it is anticipated that autopsies in persons with trait will always demonstrate sickling. The important question is whether the sickled cells found after death result from or are the cause of death. This question can be answered only by epidemiologic studies rather than by individual case descriptions.

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An extensive study of persons with the sickle hemoglobinopathies was carried out for the Armed Forces by a special committee of the Division of Medical Sciences of the National Academy of Sciences at the instigation of the Surgeon General of the U.S. Department of the Army following the report of Jones et al.[2] This report (published in February 1975)[4] summarized the data in regard to the sudden death syndrome as follows: "After exhaustive review of the literature and the study of data made available to the committee by the Armed Forces and the Veterans Administration, the committee found no scientific basis to implicate the sickle cell trait in the sudden death syndrome as has been suggested by Jones et al. The spleen and kidney undoubtedly are the only organs for which the relation of disease and sickle cell trait is well established. With regard to other organs, the association is based on isolated reports." In another section the committee states that "there must be other yet unknown contributory factors not necessarily related to the sickle cell trait that makes some persons susceptible to collapse or sudden death."

Furthermore, the clinical and laboratory manifestations of the sudden death syndrome that were observed in the Colorado football player and in the patients reported by Jones et al[2] were similar to those caused by exertional rhabdomyolysis.[5] It has been postulated that the renal shutdown and marked acidosis of severe rhabdomyolysis might cause preterminal sickling in persons with trait.[6] The present evidence suggests that exertional rhabdomyolysis which may occur in a severe form for unknown reasons in certain individuals may be one of the primary causes of unexplained sudden death in athletes. There is no evidence, however, that sickle cell trait makes persons more susceptible to rhabdomyolysis and there appears to be no evidence that altitude plays any role in this syndrome.

Further reassurance that there is no proved relationship between the sudden death syndrome and sickle cell trait and altitude is provided by the fact that 6.7 per cent of the black players of the National Football League have sickle cell trait and have not demonstrated any special health problems with heavy exertion during games played at various altitudes.[7] There were also no reports of complications of this type among the black athletes participating in the Mexico City Olympics at an altitude of 7,000 feet.[8] Thus, there now appears to be no epidemiologic evidence to indicate that persons with sickle cell trait are at increased risk of sudden death in association with exposure to either altitude or physical exertion.

It is also of interest that the sudden death syndrome (characterized by acute renal failure and acidosis) has not been described in association with sickling crises in persons with various forms of symptomatic sickle cell disease such as sickle/thalassemia, sickle/hemoglobin C, and sickle cell anemia following physical exertion or at high altitude.

Splenic Sequestration Syndrome

One clinical syndrome, however, has been clearly documented in persons with sickle hemoglobin exposed to high altitude. This is the splenic sequestration or splenic infarction syndrome which is characterized by the sudden onset of severe left upper quadrant pain, anorexia, and vomiting. Physical examination shows a tender enlarged spleen and often a rigid abdomen with rebound simulating an acute surgical abdomen. The laboratory findings include anemia, leukocytosis with a shift to the left, and frequently thrombocytopenia. Spleen scans have shown definite large infarcts in some cases or simply hypofunction associated with sickle cell sequestration in the spleen in others. In some cases pulmonary infarcts and/or pleural effusion have also been noted.

In a recent review of the literature[1] we have found reports of forty-six cases of splenic infarction or sequestration causing symptoms in persons with sickle hemoglobin after exposure to high altitude. We have observed five additional cases in children with sickle/Hgb C disease, in which splenic sequestration was triggered by altitude, bringing the total reported cases of this syndrome to fifty-one.

The specific types of sickle hemoglobinopathies in these reported cases are:

"Sicklemia"*	10
Sickle cell trait (proven) -A/S	9
Sickle cell trait (probable)-A/S**	12
Sickle/Hgb C-S/C	17
Sickle thalassemia- S/thal	3
Sickle cell anemia-S/S	0

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*"Sicklemia"—represents cases with positive sickling but not studied by hemoglobin electrophoresis. May include S/A, S/C, S/thal.

**Sickle cell trait (probable)—represents cases with S and A hemoglobins by electrophoresis but not studied quantitatively to differentiate sickle cell trait from sickle/thalassemia.

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The previously reported cases occurred primarily with travel in unpressurized aircraft flying over the Rockies at altitudes of 10,000 to 15,000 feet, and only four cases are described in association with mountain travel or recreation. Three of these were proven to be in persons with sickle cell trait. Four of the five cases observed by us in S/C disease[1] were associated with high mountain travel or hiking.

Sickle Cell Trait and Altitude

The incidence of splenic sequestration or infarction in persons with sickle cell trait at high altitude must be extremely low since there are only twenty-one cases reported in the literature and only nine of these were proven by quantitative hemoglobin electrophoresis to have sickle cell trait. The reports also suggest that very high altitude is usually necessary to precipitate this type of crises. The majority of cases have occurred during aircraft flights in unpressurized planes at altitudes between 10,000 and 15,000 feet.

The circumstances of four previously reported examples of splenic infarction at mountain altitudes in three persons with sickle trait and one with "sicklemia" were as follows: (1) following an automobile trip over the Rockies and Sierras—in a white male with "sicklemia" (not studied by electrophoresis),[9] (2) after driving over a 15,000 foot pass in the Andes—in a white Peruvian male with sickle cell trait,[10] (3) while climbing Mt. Washington at 2,500 feet—in a white man (of Sicilian background) with sickle cell trait,[11] and (4) after visiting the top of Pikes Peak at 14,000 feet—in a black male with sickle cell trait.[12] Two of these cases were at very high altitudes (14,000 and 15,000 feet) and only one example has been reported in persons with trait at a relatively low altitude (2,500 feet on Mt. Washington). The high proportion of white persons with sickle cell trait in these reports is of interest and has raised the possibility that the risk of developing the splenic infarction syndrome at high altitude may be greater in whites with sickle cell trait than in blacks with the trait.[13] One further case was reported from Alamosa, Colorado at 7,500 feet in a black athlete with sickle cell trait. However, he had also flown to Colorado that same day in an unpressurized plane at 11,000 feet.[14]

We are aware of a number of instances of black persons with the trait being exposed to high altitudes by skiing at 11,000 to 12,000 feet and visiting the top of Pikes Peak and Mt. Evans by car without incurring any symptoms suggestive of the splenic sequestration syndrome or any other type of sickling crisis. It is our impression that this complication is quite rare in blacks with sickle cell trait in association with mountain travel or recreation. However, more specific data is needed to answer the question of the exact incidence.

The only clearly proven morbidity associated with sickle cell trait appears limited to the spleen, lungs, and kidneys. It has been well documented that persons with sickle cell trait may develop hyposthenuria and rarely may demonstrate hematuria. There is no data to indicate that altitude plays any role in these minor renal complications. The life expectancy of persons with sickle cell trait has been shown to be normal[4] and progressive renal disease has not been documented at the present time.

Sickle/Hemoglobin C Disease and Altitude

Review of the literature[1] shows that 33 per cent of the reports of the splenic sequestration syndrome have been in persons with sickle/hemoglobin C disease (S/C). When one compares the incidence of S/C disease with that of sickle cell trait in the black population (1 in 2,000 as compared with 1 in 12), the risk of splenic sequestration in S/C disease appears to be much higher than in sickle trait.

We have recently observed five such patients in Colorado.[1] All were black children with proved sickle/hemoglobin C disease, and all presented with a classical picture of a splenic sequestration crisis. Spleen scan was carried out in two of the five and demonstrated splenic hypofunction suggesting sequestration but did not show large infarcts. Four of the five were hiking or camping in the Rocky Mountains at altitudes above 9,500 feet when the crisis occurred. One of the four had moved ten days previously from Los Angeles to the Denver area by pressurized plane.

It is our impression from this experience and from the review of the literature that persons with sickle/hemoglobin C disease are at definite risk of developing the splenic infarction syndrome at high altitude in the mountains or even with a change in altitude from sea level to Denver. This impression is supported by the fact that crises have occurred in pressurized aircraft (estimated comparable to an altitude of 5,000 to 7,000 feet) in four persons or in unpressurized planes at 4,000 to 6,000 feet altitude in two others.[15] On the other hand, we are also aware of individuals with sickle/hemoglobin C disease who have traveled into the Rockies above 9,000 feet and who have flown in pressurized planes without developing symptoms.

Sickle/Thalassemia and Altitude

A total of three cases of splenic infarction syndrome have been reported in black persons with sickle/thalassemia in association with exposure to high altitude through aircraft travel. Two of these were in unpressurized planes at altitudes above 10,000 feet[15,16] while one was in a plane pressurized to the 5,000 to 7,000 foot level.[8] We are not aware of any persons with sickle thalassemia having had symptoms at high elevations in the Rocky Mountains. The incidence of this hemoglobinopathy is much lower than sickle trait or sickle/hemoglobin disease. However, the occurrence of the splenic sequestration complication with altitude in persons with sickle/thalassemia may be more common than has been recognized, because of the difficulty in differentiating sickle/thalassemia from sickle trait even by hemoglobin electrophoresis. Quantitative determinations must be done since both conditions have A and S hemoglobins.

Sickle Cell Anemia and Altitude

There has been a long-standing impression that persons with sickle cell anemia are more apt to develop vaso-occlusive crises when exposed to high altitude. This has been well documented in other situations associated with hypoxia but the actual degree of risk with altitude has not been studied. There are reports of individual cases, and we are aware of patients who have developed vaso-occlusive crises while driving in the Rockies. On the other hand, we know of persons with sickle cell anemia who have traveled over 12,000-foot passes without precipitating a crisis. Again, the incidence of complications in association with various levels of altitude needs to be documented.

The splenic infarction syndrome has not been reported in persons with sickle cell anemia with altitude. This is probably due to the fact that most of these individuals undergo autosplenectomy through repeated small splenic infarcts during the first two to four years of life. The young child who still has splenomegally would be the one potentially most susceptible for development of this complication in association with hypoxia.

Summary

There is good evidence from the extensive study carried out for the Armed Forces that the sudden death snydrome with physical exertion is not caused by sickle cell trait (even at high altitude).[5] It is also not characteristic of other sickle hemoglobinopathies. There is increasing evidence that one cause of this syndrome may be rhabdomyolysis. It is not known whether persons with sickle cell trait have greater complications if they develop rhabdomyolysis.

The splenic infarction syndrome may be characterized by either significant large infarcts or splenic hypofunction due to sequestration of masses of sickled cells. It has now been well documented in persons with sickle cell trait, those with sickle/hemoglobin C, and sickle/thalassemia. There is good evidence that this type of crisis may occur in association with altitude. It would appear that the risk is greater with sickle/hemoglobin C disease than with any of the other sickle hemoglobinopathies. Pulmonary infarcts may also occur but have been reported only in assocation with the splenic infarction syndrome at high altitude. Other types of vaso-occlusive crises have been reported at high altitude only in persons with sickle cell anemia.

It is clear that an epidemiologic study is needed in order to delineate the true incidence of complications in persons with the sickle hemoglobinopathies who travel in the Rocky Mountains.•

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Coronary artery obstruction due to blunt trauma

M. L. Laman, MD, Pueblo, Colorado and
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A case of complete obstruction of the left anterior descending coronary artery due to blunt trauma in a 35-year-old-housewife is reported.

Anterior chest trauma is a common event resulting in a variety of injuries. Blunt trauma to the heart resulting in coronary artery occlusion is not commonly reported and a cause and effect relationship between the blunt chest injury and the artery obstruction may be difficult or impossible to prove. This case report, we believe, represents complete obstruction of the left anterior descending coronary artery following such blunt trauma.

CASE REPORT

In September, 1971, a slender 35-year-old premenopausal white woman was in an automobile accident and was thrown against the steering wheel. She was seen in the emergency room at her hometown hospital in Massachusetts, and fractures of the nose and one metacarpal were noted. X-rays of the skull, chest, knees and right wrist were said to be normal and an electrocardiogram was not done. In June, 1972 while undergoing a vaginal hysterectomy, she developed intermittent left bundle branch block (Fig. 1) during general anesthesia (Pentothal, Nitrous oxide and Fluothane).

The past medical history indicated that the patient had suffered from recurrent asthmatic attacks as an adult that had decreased markedly in frequency since moving to Colorado. A previous electrocardiogram in October, 1970, showed non-specific ST segment and T wave changes. She had never been a cigarette smoker and gave no history of diabetes, hypertension, or lipid abnormalities in herself or her family. She was not on birth control pills.

Blood pressure was 128/70 and the pulse 70. Examination of the heart was within normal limits. There were no signs of enlargement and there were no murmurs, thrills or third or fourth heart sounds. The remainder of the physical examination was unremarkable. A chest X-ray was normal as were the lipids and a glucose tolerance test after a three day carbohydrate diet prep. Serial electrocardiograms and enzymes (CPK, SGOT, LDH) over the next several days failed to show any abnormality except the intermittent left bundle branch block which was not rate-related. Her postoperative course was uneventful, and she was discharged.

An exercise treadmill test was attempted in November, 1972, (Fig. 2), but was terminated with the development of left bundle branch block. The exercise test produced no symptoms. She was seen in the emergency room later in November, 1972, with chest pain and an electrocardiogram was unremarkable. Because of the recurrence of chest pain suggestive of angina pectoris, she was admitted to Penrose Hospital in Colorado Springs in January, 1973. Selective coronary arteriograms during that admission revealed complete obstruction of the left anterior descending coronary artery. (Figs. 3 and 4.) The other vessels and the left ventricular function were normal.

Since that time the patient has continued to have rare episodes of exertional chest pain and was admitted to the hospital in February, 1973, and September, 1973. Each time serial electrocardiograms and enzymes have failed to show changes of a myocardial infarction.

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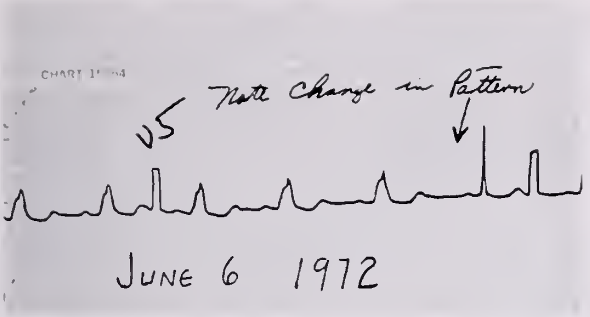

Fig. 1. Intermittent left bundle branch block on a postoperative monitor strip.

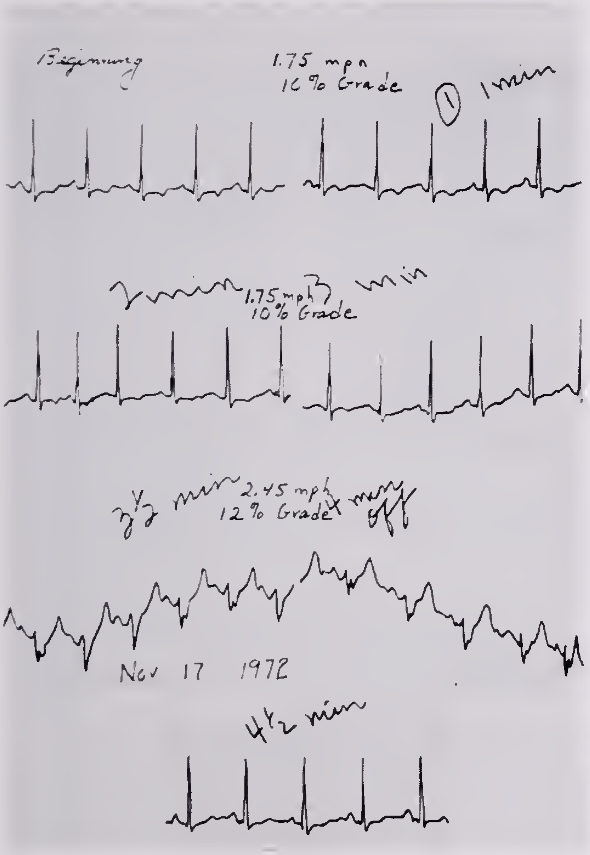

Fig. 2. Appearance of left bundle branch block during treadmill testing.

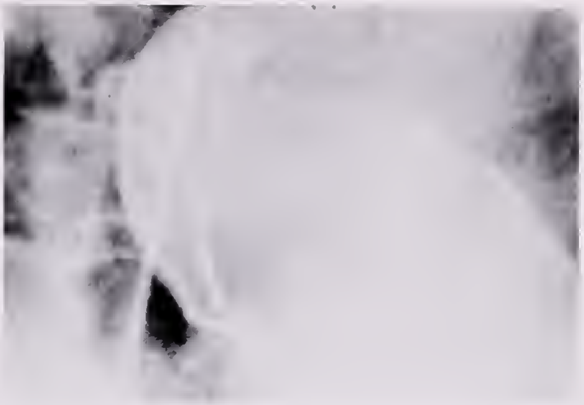

Fig. 3. Cineangiogram frame in the left anterior oblique projection showing absence of the left anterior descending vessel.

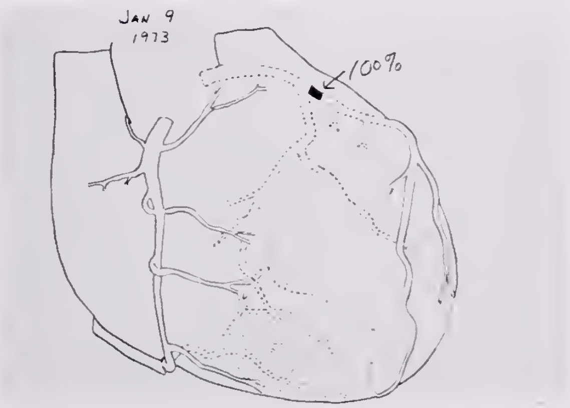

Fig. 4. Diagramatic representation of the complete obstruction of the left anterior descending vessel in the right anterior oblique projection.

Summary

An example of coronary artery obstruction secondary to blunt anterior chest trauma is presented. The normal angiographic appearance of the remaining coronary vessels, the absence of any risk factors, and the fact that the patient was premenopausal at the onset of symptoms all strongly support the position that blunt chest trauma was the cause of the obstruction. ●

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Acute posttraumatic anterior ankle instability

*H. M. Frost, MD and C. A. Hanson, MD, Pueblo**

HYPERMOBILITY OF THE ANKLE in the anterior direction has long been known to occur in paralytic situations which exist during growth, and to a lesser degree in paralytic situations arising in adult life. However, Landeros and Frost in 1966[1] drew attention to this type of ankle instability as a common consequence of acute trauma. Since that article, a number of papers by other authors have dealt with this entity, confirming its existence and adding to our knowledge of its pathology and pathomechanics. This report summarizes the authors' personal experience with the syndrome over a collective total of 34 years of practice. While both acute post-traumatic and chronic post-traumatic anterior ankle instability syndromes exist,[2] this report concerns solely the acute form. The acute form, while clearly the most common type of acute ligamentous ankle instability, still is not widely recognized.

Typical History and Findings

The typical patient, under 30 years of age, has sustained an acute ankle injury, usually of the supination-adduction variety. He complains of pain and swelling in the region of the lateral malleolus of the ankle. Tenderness exists over the anterior talofibular ligament and also over the anterior portion of the deltoid ligament somewhere along its cephalocaudad course. Commonly, x-rays of the ankle are normal except for soft tissue swelling, usually over and about the lateral malleolus and occasionally over and about the medial malleolus. Table 1 lists the typical symptoms and signs.

The specific test for this condition—the anterior drawer sign of the ankle—described by Landeros and Frost is quite reliable but *must* be performed properly to elicit a positive test.[2] The patient should be seated on the edge of the examining table or lying down, and the knee on the involved side should be flexed to 90 degrees. It is absolutely essential that the musculature actuating the ankle be relaxed. Even with completely torn ligaments, one may not demonstrate a positive anterior drawer sign if the patient tenses the anterior tibial, gastrocnemius, and soleus muscles.

To examine the left ankle, the physician places the heel of his right palm over the anterior tibia immediately proximal to the ankle joint. The index finger lies on the posteromedial talus, while the middle finger lies on the posterior medial aspect of the medial malleolus. The left hand is placed with the palm against the sole of the foot and the fingers curled around the heel. The ankle must be positioned at a right angle to the leg, for one usually cannot demonstrate a positive drawer sign in a plantar flexed ankle. One then pushes posteriorly on the tibia with the right hand while simultaneously he pulls forward on the heel with the left hand, using the index and middle fingers of the right hand to feel any relative motion between the posterior tibia and the posterior talus. Fig. 1 illustrates the above maneuver. Normally, some slight anteroposterior play exists, so that in evaluating a positive sign, one must compare the injured ankle to the normal ankle. Test the right ankle in mirror image fashion to that described for the left. Table III provides information on the amount of anterior motion found in normal ankles. Observe that in this respect children's ankles are quite lax and with age this laxity diminishes considerably.

Anterior motion of the talus in the ankle mortise of ¼ inch or more (*i.e.*, > 6 mm) in an adult is abnormal in 95 per cent of otherwise healthy subjects. Care must be taken not to mistake chronic anterior instability for acute instability. This requires appropriate inquiry into the history, and sometimes one simply cannot draw reliable conclusions about the origin of a positive drawer sign, particularly when much anterior motion exists in the presence of relatively little pain and if accompanied by little tenderness and no swelling. If required for purposes of documentation, lateral x-rays of the ankle can be taken while performing the anterior ankle stability test. (See Figs. 2a and 2b).

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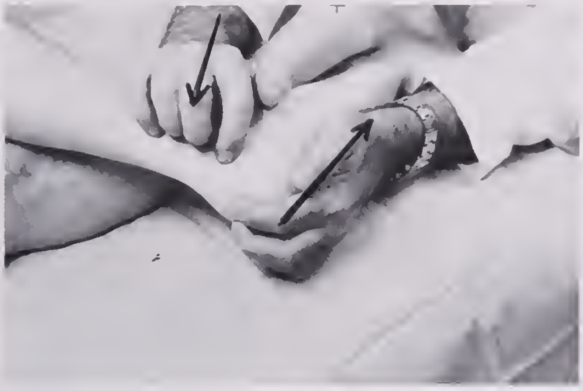

Fig. 1. Technic for eliciting the anterior drawer sign of the ankle.

For the talus to come forward to a pathologic degree in the mortise, two conditions must exist. First, the talus must displace caudad, as a brief inspection of the geometry of the relevant anatomy in Figs. 2a and 2b shows, and for this to occur, the deltoid ligament must be either lax or torn. Second, to permit anterior subluxation of the talus, the anterior talofibular ligament must be either lax or torn.

In the authors' experience, this injury is fairly common. Currently, an average of two new cases a month is seen in a two-man general orthopaedic practice in a medium-sized city. While this injury may also be associated with stretch or tear of the inferior talofibulocalcaneal ligament, the latter injury presents only ten per cent as frequently as the pure anterior instability. Note that anterior instability may coexist with other acute injuries, as shown in Table 3. If extremely painful, these other injuries may distract the attention of both patient and physician from the pathology of the coexisting anterior instability, leading to a missed diagnosis. By far the most common cause of chronic instability is a missed original diagnosis.

Treatment

The acute posttraumatic anterior ankle instability should be treated with a non-weight bearing long leg cast with the knee flexed approximately 30 degrees and the ankle at a right angle. The cast must be worn for 6 weeks. More than 95 per cent of the acute injuries so treated should have a perfectly snug ankle at the time of cast removal, and these ankles should remain snug during subsequent rehabilitation and after return to normal activity. (See Table 4).

It has *not* proven necessary to do routine open ligament repair on acute, posttraumatic anterior unstable ankles.

TABLE 1

Acute Posttraumatic Anterior Ankle
Instability

Symptoms and Findings
(123 Ankles)

Symptoms	% of Cases
History of acute ankle injury	96*
History of previous ankle injury	15
Pain in the lateral malleolar region	100
Pain in the medial malleolar region	30
Pain elsewhere in the ankle/foot	30

Findings	% of Cases
Swelling over and about lateral malleolus	100
Swelling over and about deltoid ligament	70
Tender anterior talofibular ligament	98
Tender anterior deltoid ligament	75
Positive anterior drawer sign	100

*Four per cent were found in patients with multiple severe injuries sustained in industrial and motor vehicle accidents who either were comatose or had no specific recollection of an ankle injury.

However, when anterior instability accompanies a tear of the inferior fibulocalcaneal ligament, we (in agreement with S. Staples[3]) do perform early open ligament repair. Postoperatively, the ankle must be immobilized for 6 weeks in a non-weight bearing long leg cast, with the knee flexed approximately 30 degrees and the ankle at a right angle.

Results

Table 4 summarizes the results at 6 months or more after injury of 123 acute posttraumatic anterior unstable ankles seen and treated from the outset by the authors. In essence, about 96 per cent of the 90 properly cast patients and 87 per cent of the 15 operated patients had excellent results. In contrast, only 11 per cent of those cases not cast at all or improperly cast had stable ankles; and approximately three-fourths of those patients had persistent ankle symptoms.

Table 5 summarizes the causes of therapeutic failures in 135 acute posttraumatic anterior unstable ankles. One hundred fifteen of these ankles were seen and treated originally by other physicians, and only at some later time were they seen by the authors. The other 20 ankles were originally seen and treated from the outset by the authors. The therapeutic failures fall into the following categories:

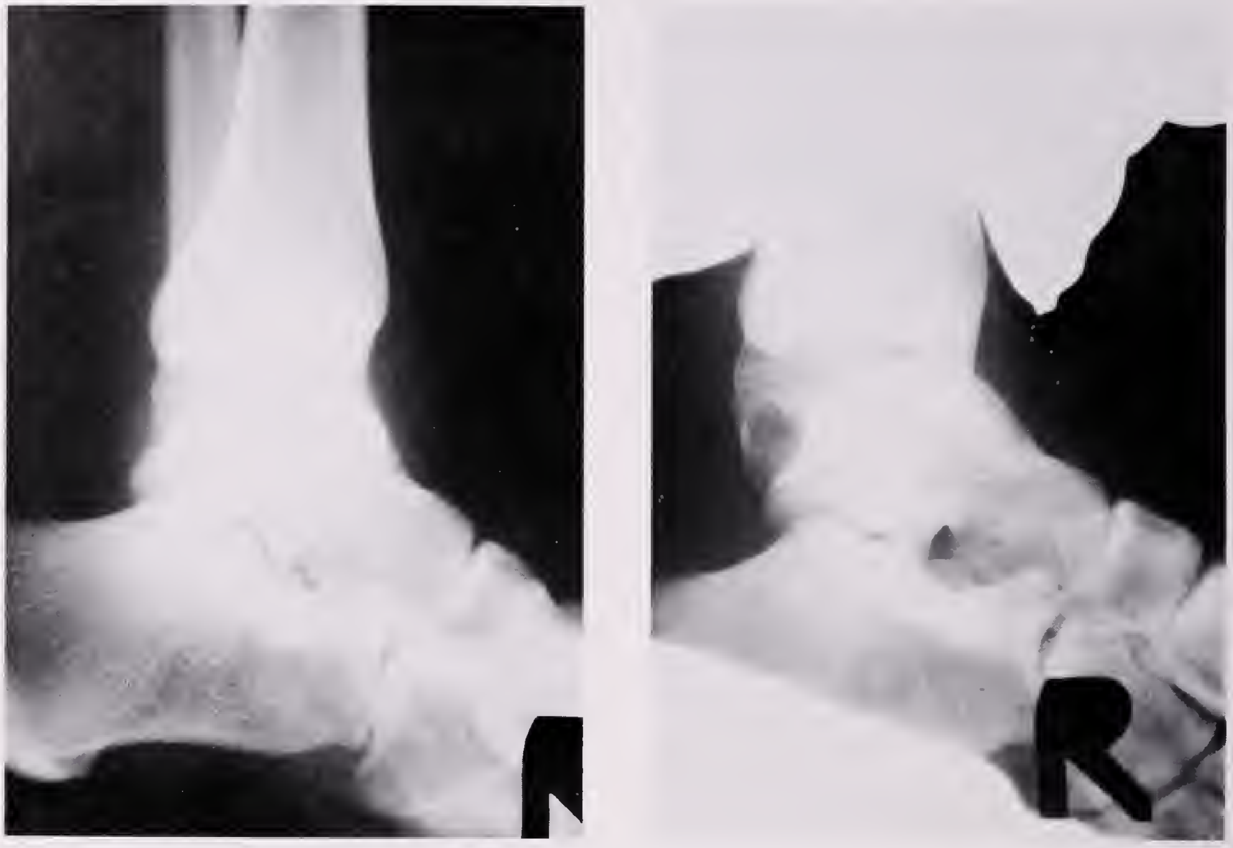

Fig. 2. X-rays taken while performing the anterior ankle stability test. (a) no anterior stress. (b) anterior stress with positive drawer sign.

(1) Approximately one patient in twenty with acute anterior ankle instability alone who is treated as we recommend with a non-weight bearing long leg cast for 6 weeks, will demonstrate a positive drawer sign 6 months or more later. The other 95 per cent of these patients should retain an objectively snug and functionally normal ankle. The causes for this 5 per cent failure rate are conjectural at present.

(2) Failure of treatment can occur when chronic anterior ankle instability caused by a former injury or injuries is mistakenly assumed to represent an acute anterior instability when first seen after a new injury.

(3) Inadequate casting, *i.e.*, non-weight bearing short leg cast, short leg walking cast or casting for 4 weeks or less, is responsible for many failures. Fewer than 15 per cent of the patients so treated have a negative anterior drawer sign six months later. This has been equally true whether the acute injury was treated entirely closed, or was subjected to immediate open ligament repair followed by application of a short leg walking cast. The explanation for this situation may lie in the fact that the short leg cast cannot control torque of the foot on the leg, and as a consequence, normal, inadvertant, and frequent internal and external rotation of the

TABLE 2

Acute Posttraumatic Anterior Ankle Instability

Anterior Talar Motion in the Ankle Mortise in Normal Subjects*

Age Group (years)	(n)**	Mean (mm)	Range in the central 66% of the group (mm)
0 - 10	(9)	5	3-8
11 - 20	(16)	3	2.5-7
21 - 40	(12)	2	1.5-5
41 and older	(15)	1.5	0.5-4

*These previously unpublished data were determined on x-rays of normal ankles at Henry Ford Hospital, Detroit, Michigan, by H.M. Frost, MD, and O. Landeros, MD, in the years 1963-1967.

**Number of normal ankles in the group. Note: after age 12, females consistently demonstrated 1-2 mm greater motion than males.

TABLE 3

Acute Posttraumatic Anterior Ankle Instability

Other Pathology Found in Same Ankle/Foot (123 Ankles)

Name of Pathology	% of Cases Found In*
No other pathology recognized	85
"Y" ligament sprain	5
Tear of inferior fibulocalcaneal ligament	10
Fracture of lateral malleolus	7
Fracture of medial malleolus	4
Fracture of one or more foot bones	3
Laterally unstable mortise (mostly tears of the distal tibiofibular ligaments)	3

*Because of some overlap, the sum exceeds 100%

foot on the leg twist the talus in the mortise, thereby stretching the ligaments and/or the sutures. Note—after one week in plaster, even one single twist of the talus in the mortise can tear or pull out sutures and cause the ligaments to heal with laxity.

(4) The most common cause of failure (*i.e.*, a chronically anterior unstable ankle) was failure to diagnose the original injury correctly, and therefore absence of any effort to treat it.

Chronic anterior instability due to a former injury which either was not treated properly or which failed to respond to treatment generally held to be proper, is a separate problem and will not be dealt with here. However, for the present purposes, we may report that this is a significant problem primarily in athletically active adolescents and young adults. As people become older and more sedentary in their physical habits, the amount of discomfort and disability attributable to this injury usually declines dramatically, and one rarely sees a patient over 50 years of age who has disability attributable to this phenomenon. When one compares that fact to the relative frequency with which one sees the condition as an acute injury in younger people, one must infer that the disability tends to be strongly self-limiting. Indeed, this was a major factor in our decision to attempt to treat the majority of these acute injuries by some non-operative means.

TABLE 4

Acute Posttraumatic Anterior Ankle Instability
Results
(Authors' personal series of 123 ankles)

Group	(n)	Objectively tight ankles, 6 months later.% of group	Subjectively normal ankles % of group.
I. Refused casting or not treated for other reasons:	9	11	22
II. Short leg walker cast, non-weight bearing short leg cast, or any casting less than 4 weeks.	9	11	22
III. Non-weight bearing long leg cast with knee flexed approximately 30 degrees X 6 weeks.	90	96	96
IV. Early operative repair of ligaments:followed by non-weight bearing long leg cast with knee flexed approximately 30 degrees X 6 weeks.	15	100	87

TABLE 5

Acute Posttraumatic Anterior Ankle Instability
Causes of Therapeutic Failures
(135 ankles)

Causes	% of All 135 Poor Results
Lesion not originally diagnosed correctly	78
Inadequate casting.	14
a) Non-weight bearing short leg cast	
b) Short leg walker cast	
c) Long leg walker cast	
d) Casting for four weeks or less	
Postoperative infection	1
Patient refused to follow through with treatment.	2
Cause unknown (possibly unrecognized chronic instability antedated the most recent injury which was recognized and treated).	5

Conclusions

1) The syndrome of acute posttraumatic anterior ankle instability is described, as well as the technic for performing the test for the anterior drawer sign of the ankle, the test which specifically demonstrates that form of instability.

2) Although not yet widely recognized, this syndrome is the commonest form of post-traumatic ankle instability. It outnumbers by 10 to 1 the lateral tilt of the talus in the mortise which is discussed in detail in standard operative texts.

3) Treatment with non-weight bearing long leg cast with the knee in flexion and the ankle at a right angle for 6 weeks produces 95 per cent subjective and objective cures.

4) In our experience, the two most common causes of chronic anterior ankle instability are (a) failure to recognize, and thus to treat, the acute form, or (b) use of short leg casts, or the use of any type of cast for less than 6 weeks.●

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Current trends in scabies*

Gerard G. Koehn, MD, Pueblo, Colorado

Scabies is increasing at a remarkable rate in the United States and abroad. The clinical characteristics and management of this infestation is presented.

For the past two years, we have experienced locally and noted throughout the United States a dramatic increase in scabies. In 1971, Orkin[1] reported a resurgence of this infestation, especially in Europe and South America. Although at that time, the epidemic had not yet reached this country, since 1971 the incidence of scabies has increased[2] to the point that dermatologists in the United States see several new cases weekly. Recently an epidemic of scabies in a town of 15,000 in Maine involved one-third of the population and closed the schools.

The prevalence of scabies through the years seems to fluctuate, with epidemics occurring at 10 to 15 year intervals, the last epidemic being in 1963-64. Because of the rarity of scabies in the intervening years, there has been a decrease in the index of suspicion among clinicians with resultant misdiagnosis and mismanagement. It is essential, then, that these recent developments be brought to the attention of all physicians. An illustrative case is described.

CASE REPORT

A 22-year-old white male was seen in the dermatology clinic for intractable pruritus of 2 weeks duration. The itching was worse at night. Others in the commune in which he was living had itching as well. The patient had been using a benzocaine aerosol preparation with no improvement.

Examination of the skin disclosed intact and excoriated papules and papulovesicles of the interdigital webs, trunk and penis (Figs. 1, 2). Scrapings of representative lesions showed scabetic organisms and eggs (Fig. 3).

The patient was treated with Kwell lotion applied every 12 hours for four applications, and Benadryl 50 mg. every 4 hours as needed for itching and Menthol ¼ %-Phenol ½ % in Lubriderm lotion. His itching and lesions disappeared eight days after initiation of therapy and he has done well since.

Discussion

This affliction is caused by a whitish hemispherical member of the mite family, *Sarcoptes scabiei* which has four pair of short legs and measures 0.2 X 0.3 mm.[3] The itch mite was discovered in 1687, and represents the first disease of man with a known cause.[4] It inhabits the stratum corneum of its only host, man. Adult mites can survive only a few days when away from their human environment.[11]

The cyclic nature of scabies may be related to two factors: human life styles and population immunity. Epidemics of scabies have been associated with wars and the conditions characteristic of wartime living. Communal living patterns and a sexual revolution might today be partially responsible for the present resurgence of scabies. Some authors feel that immunity is an important factor in scabies and that loss of immunity in the population most at risk (18-30 years of age) might account for the cyclic nature of epidemics.

Stokes, in 1937, referred to scabies as the easiest yet most difficult disease to diagnose.[5] Severe itching is the most characteristic symptom, and it is often worse at night, perhaps because the warmth of bedclothes stimulates the mite to activity.[12] The pruritus is usually noticed about two weeks after the first infestation and earlier with subsequent ones.

Patients with scabies can have a variety of skin manifestations, the burrow and vesicles being most specific. This pathognomonic burrow,

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* From the Department of Dermatology, Southern Colorado Clinic, Pueblo, Colorado 81004.

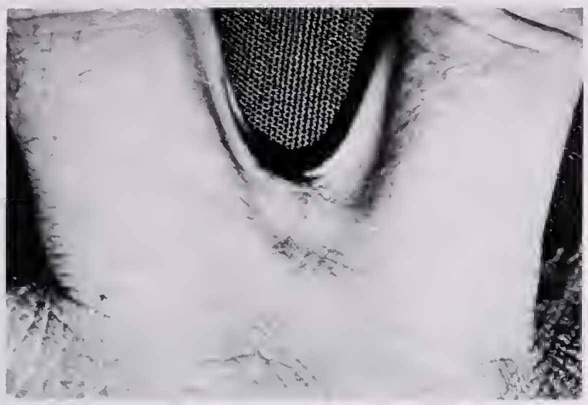

Fig. 1. Slightly excoriated papule, interdigital web.

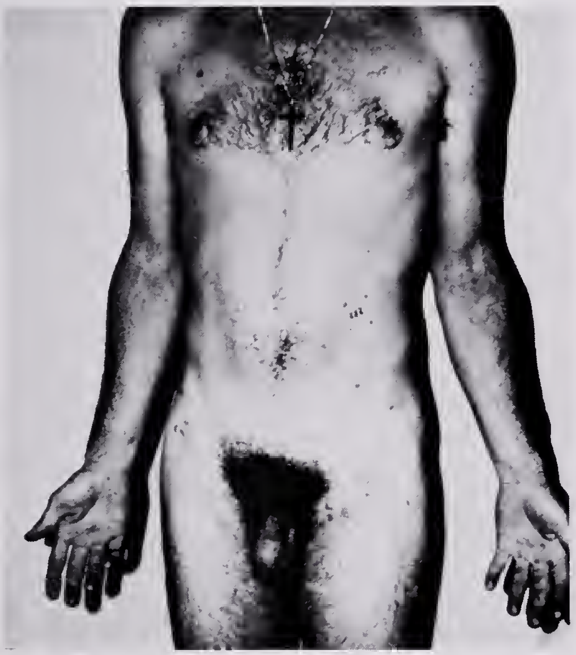

Fig. 2. Papules and papulovesicles distributed on bathing trunk area, axillary folds and penis.

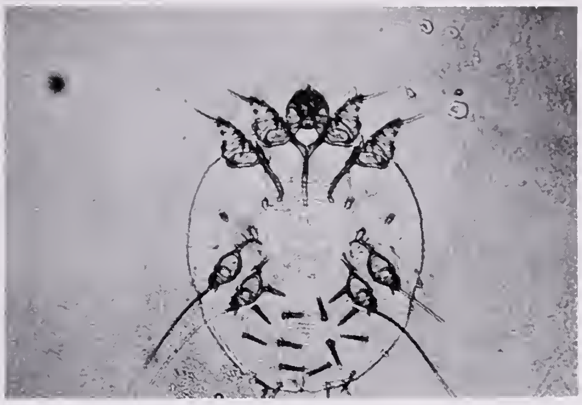

Fig. 3. Sarcoptes scabiei var hominis.

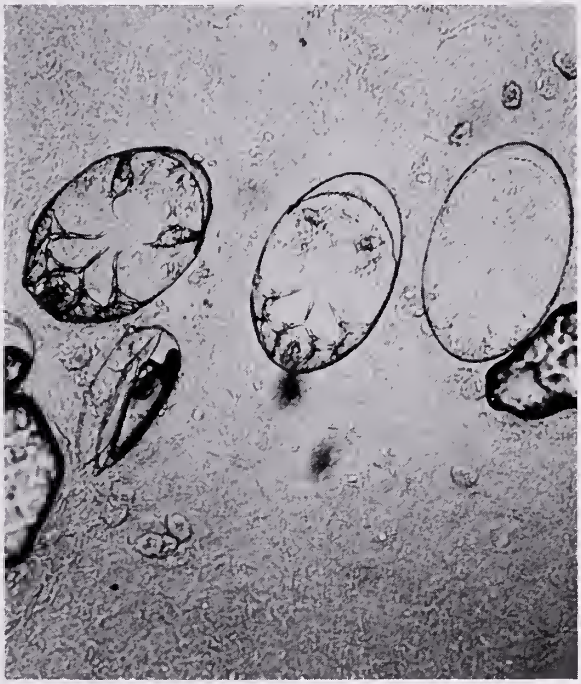

Fig. 4. Ova.

the result of the mites migration through the stratum corneum, appears as skin colored or grey ridges 5-15 mm long and often curved or S-shaped. The number of such burrows may vary considerably. In this era of hygiene and cleanliness, burrows are seen in less than ten per cent of patients. The most common location for burrows is either the volar wrist or the interdigital spaces. Urticarial and excoriated papules and nodules are reactive lesions of scabies and often dominate the clinical picture.

Distribution is important in making the diagnosis especially in the absence of burrows. The disease favors the wrists, elbows, anterior axillary folds, areolae, genitals, buttocks and hands, particularly the ulnar and interdigital surfaces. In infants with scabies, the distribution of lesions differs from that seen in adults, often occurring on the palms, soles, neck, and head.[6]

To confirm a clinical suspicion of scabies, burrows and vesicles should be scraped with a #15 scalpel blade after placing a drop of immersion oil on the lesion. Several lesions should be scraped to improve the yield of positive slides. Scrapings are then examined under the low power of the microscope. The presence of the mite, egg, or feces establishes the diagnosis. Unfortunately, better than half of these scrapings are negative. If the lesions and distribution are suggestive, antiscabetic treatment is nevertheless warranted. It has been stated that lesions itching at the time of examination[7] produce a better yield of positive scrapings. Also, the debris under the fingernails is a fertile area to find the mite. Occasionally a skin biopsy is helpful because of characteristic microscopic changes in scabetic lesions.[8]

Various factors can alter the clinical appearance of scabies, placing it in the category of syphillis and sarcoidosis as an impersonator of other diseases. It can be confused with dermatitis herpetiformis,[13] pemphigoid,[14] atopic dermatitis, neurodermatitis, mastocytosis, neurotic excoriations, impetigo and erythema multiforme, to mention only a few. The prior use of corticosteroids can change the clinical presentation of scabies making it unrecognizable. Norwegian scabies is a rare form of the affliction seen in predisposed individuals. There are often generalized warty crusted lesions with sometimes up to 2 million mites present. These patients often have Down's syndrome or other forms of mental deficiency. Absent or reduced pruritus has been observed in these patients which may favor heavy infestation. Moreover, this type of scabies has been seen in persons with severe systemic disease such as diabetes mellitus and leukemia and during prolonged systemic and immunosuppressive therapy.[3]

Several effective scabieticides are available. The most commonly used preparation in the United States is gamma benzene hexachloride 1% (Kwell® lotion, cream and shampoo). The patient is provided with 4 oz. of the lotion and told to take a warm bath or shower at bedtime and then apply the solution to all body surfaces below the neck. The lotion application is repeated every 12 hours three or more times and then followed by another warm shower or bath 12 hours after the final application. All other persons living with the patient should be similarly treated with Kwell. Other scabeticides may be utilized in the future since there have been increasing numbers of scabies resistant to gamma benzene hexachloride, especially in the northeastern part of the United States.[2] Crotomiton (Eurax) or sulfur 10% ointment are suitable alternatives.

It is important to forewarn the patient that itching may persist as long as 3 weeks after treatment and that the anti-scabetic lotion should not be continued for this period. In fact, some patients will complain of moderate to severe pruritus with papules and nodules for several weeks to months after treatment.[9,10] In patients with such forms of nodular scabies intralesional triamcinolone (5 mg./cc) or even excision of persistent itching nodules is sometimes effective. An antipruritic lotion such as Menthol ¼%-Phenol ½% in an emollient base such as Lubriderm® or Eucerin®, as well as an antihistamine way be used.

Conclusion

Scabies is becoming a major dermatologic problem in this country, and the number of cases is increasing at an amazing rate. Its presentation can be confusing, especially if modified by previous topical or systemic corticosteroids. Accepted treatment is proving resistant in a growing number of cases. It is important that the family practitioner as well as the specialist be aware of these trends.●

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RORER

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Governor Lamm, Saturday luncheon speaker, at the Rural Health Conference visits with Doctor Stephen Barnett and Doctor S. Jack Locke, chairman of the CMS Committee on Rural Health.

Doctor Joseph S. Pollard of Colorado Springs, newly installed as President of the Colorado Medical Society, presided over the Saturday luncheon at the Rural Health Conference.

Doctor Hughes Andrus from the University of California Medical School at Davis spoke on Problem Areas and Solutions in Rural Health Care Delivery Friday morning.

Doctor Grady Stumbo of Hindman, Kentucky spoke to the Friday luncheon about his experiences providing rural health care to the hill people of the Eastern seabord.

COLORADO

A SHOW OF INTEREST

Providing the best health care possible in rural Colorado was the concern of the First Rural Health Care Conference, sponsored by the Colorado Medical Society and imaginatively organized by its Rural Health Committee at Colorado State University in Fort Collins on October 23-25. To establish priorities among the many rural health needs and to consider what exists as a workable basis for a strengthening movement, approximately 350 people came through snow and slush. They came from plains and mountain valleys, Rangely and Craig, Springfield and Lamar, to join minds. They came to address how Colorado can best achieve adequate health care where numbers are small—where local energies are not large and government can wield a heavy hand.

The people represented varying conditions and different needs. To balance them off in affirmative movement there was time for talk and interchange of ideas. As a resource person for the Conference, representing the Locations Department of the Colorado Medical Society, I was familiar with the steady flow of medical personnel in and out of smaller communities, with the seemingly universal desire to practice medicine in Colorado, yet I needed information to further clarify the Department's effectiveness.

In order to take part in the conference, I found my way to one of four groups seated around tables in a large room and introduced myself to Bob Drennan, director of continuing education at the Weld County General Hospital in Greeley. We each introduced ourselves to the others of the table, each giving his different relationship to the health field. We included a medical economist, a professional health planner, a citizen member of a state health board, an intern, a nurse, and a medical student. We were to evaluate rural health needs and produce our own order of priorities.

What values should be sought for rural health care? Is it possible to attain acceptable unity of thought with so many diverse kinds of thinking? One person thought the community should above all be independent of federal and state controls. Another suggested a community must have certain essential resources. Another posed the possibility of alternatives as needed. To another nutrition was of high importance—housing—or job satisfaction. Consumer participation and control mean the result will have a democratic character. Without healthy economic growth a community is grounded. There is need for a sense of community. What is done must be affordable, subject to what can reasonably be achieved.

How could these ideas be implemented? What are the goals? From so many suggestions it was necessary to bring order. Observed one, "it's like going into Baskin-Robbins". A needed goal, perhaps the dominant one, was instillation of health values in children at school, and through a continuing health education program. Health care must be within reach.

There are many considerations—participation of consumers, health promotion, communication with local population, economically feasible health care, adequate resources, independence for individuals. Of all these elements, which are the most important? Were these wants compatible with a reasonable health program of proper quality? Should the consumer define this quality, or should the fund-providers—the state or federal government—define it?

Different people have distinct ideas. Professionals in the field have their own requirements. The rural resident wants to be sure his health care is in good hands—that when the time comes for emergency treatment it is there without a chain to long-term indebtedness for the community.

Five hundred problems had been identified by the end of the morning session. From the ten to twenty problems defined by each group, the top three were selected to provide the basis for discussions in afternoon efforts toward finding solutions.

The "Need for More Data on Rural Health Needs", one of twenty-one different areas of concern, first looked at funding in a rural area with a low budget, and in a second session at how to identify the health needs of a community. Individuals in this group posed solutions, after which priorities were established. Anxiety was felt that the discussions of solutions required more time to make up for the time that had been given over to the balancing of statistics.

On Saturday morning, fifteen groups, organized in terms of geographical areas of Colorado, met to implement problem-solving procedures. This discussion led to a re-investigation of the problems that had received such thorough discussion in the first of Friday's morning sessions. Stronger catalysts were needed in order to find a broader expression of general interest to oppose the narrow concerns of different interest groups.

But the heart of the Conference was in such decisions as that of one group which arranged for continuing meetings on a regular basis in an ongoing dialog.

Allen Young

Abstracts of Papers to be presented at the Annual Joint Meeting of the Colorado Region of the American College of Physicians and the Colorado Society of Internal Medicine, Colorado Springs, Colorado, January 15, 16, 17, 1976.

Cellular and Humoral Immunity in Myeloproliferative Diseases

N. J. DiBella, MD, and G. L. Brown, MD

Thirty-three patients with myeloproliferative disorders (MPD) were evaluated immunologically. Stimulation indices (SI) using tridiated thymidine in peripheral blood lymphocytes exposed to phytohemagglutinin (PHA) were significantly lower than control values in six of eight with agnogenic myeloid metaplasia, five of six with idiopathic thrombocythemia, six of six with chronic myelocytic leukemia, two of two with paroxysmal nocturnal hemoglobinuria, and one of two with "smoldering" or preleukemia. The SI valued in five of eight patients with polycythemia vera were lower than the controls (SI 70-150) but not as depressed as in the other MPDs, with a median SI of 54. Despite low SIs in most patients with MPD, twenty-four of twenty-six tested had a normal skin test response to at least one of four antigens.

Ten of these thirty-three patients had received cytotoxic therapy within six weeks of this immunologic evaluation, yet no direct relationship could be established between this therapy and the depression in response to PHA. The mean values for serum IgG, A, M, and C'3 were normal. Severe depression of all immunoglobulins was noted in one patient with advanced myeloid metaplasia. Several others in the various diagnostic categories exhibited very high or low Ig levels, but there was no consistent trend. Thus we have demonstrated no specific changes in immunoglobulins, normal cutaneous reactivity, and depressed lymphocyte response to PHA in patients with myeloproliferative diseases.

True Muscular Hypertrophy and Hypothyroidism

Janet Schemmel, MD and Michael Cherington, MD

True, non-physiologic, muscular hypertrophy is an unusual medical disorder. Its uncommon association with congenital and childhood hypothyroidism has been documented by Bruck, DeLange, Debré and Semalaine, Hall, et al and Cross, et al. In these cases, muscle weakness and easy fatigability were described. Adults with this muscle disorder have muscle pain, weakness and pseudomyotonia, described by Hoffman, Woods, Spiller, Fay, Hesser and Walton. We have followed a case of True Muscular Hypertrophy, in which muscle strength was excessive, and no myotonia was present. Primary hypothyroidism was documented, and, after thyroxine therapy, muscle hypertrophy decreased slowly and gradually. Concomitant glucose intolerance also improved. This unusual patient and a review of similar reports will be presented.

Carcinoma of the Lung Associated with Hyperamylasemia

J. Roller, MD and W. R. Brown, MD

Hyperamylasemia and hyperamylasuria have been observed in patients with carcinoma of the lung. In at least one such case, salivary isoenzyme of amylase was extracted from the tumor. We have studied a 78-year-old white man with biopsy proven adenocarcinoma of the lung, and no evidence of pancreatic or salivary gland disease. Serum amylase was 2137 Somogyi units/dl and urinary amylase 6550 Somogyi units/dl. Isoenzyme analysis by ion exchange chromatography revealed that both serum and urinary analyses were 99 per cent salivary type and one per cent pancreatic type. Radiation therapy was followed by clinical improvement and a modest decline in amylase values.

Source of this patient's elevated amylase values, presumed to be the lung tumor, may be clarified by postmortem analysis. Ectopic production of amylase by a tumor should be considered in cases of otherwise unexplained hyperamylasemia and hyperamylasuria.

The Radionuclide Evaluation of Obstruction, Acute and Chronic Renal Disease

Thomas H. Ravin, MD, Thomas A. Verdon, MD and Frederick R. Gydesen, MD.

Radionuclide evaluation of renal disease is having a small revival because of recent developments in equipment and in radiopharmaceuticals. The gamma camera and recent introduction of ^{99m}Technetium-Tin-DTPA have expanded the evaluation of renal disease by affording a non-invasive and rapid procedure. The method used is serial five minute scan for thirty minutes using both ^{99m}Tc-Sn-DTPA and ^{131}I-Hippuran. Immediately following the injection of the former, rapid sequence images of the kidneys are obtained for a "flow study." This gives an estimation of the relative renal blood flow. ^{131}I-Hippuran is used to get gamma camera images and not for the usual renogram.

The scan images with both isotopes reflect the known pathophysiologic changes of acute (ARF) and chronic renal failure (CRF), and obstruction. The scan images in obstruction show an increased collection of radioactivity in the renal pelvis and ureters. The patient who has anuria because of ARF will have no activity in the renal pelvis or ureters. The renal parenchyma in ARF will universally show a prolonged and continually increasing amount of activity. The patient with CRF will show only a poor image. However, the scan will be useful even with elevated BUN and creatinine and it is useful in following the course of uremia in its later stages. This method is non-invasive and rapid. It is a valuable adjunct in the differential diagnosis of acute anuria, obstruction, and chronic renal failure.

Hypocalciuric Effect of Lithium in Man

Paul D. Miller, MD, Steven L. Dubovsky, MD, Keith M. McDonald, MD and Robert W. Schrier, MD

Urinary Ca++ excretion was examined in six patients with affective disorders before and three to four weeks after treatment with Lithium (Li). In these patients urinary Ca++ excretion was 213±61 mg/d SEM before and 89±24 mg/d after Li treatment ($p<.025$). Two patients had idiopathic hypercalciuria and became normocalciuric on Li. This hypocalciuric effect of Li occurred in the absence of changes in urinary sodium, phosphorus, and cyclic AMP excretion. Total serum Ca++, ionized Ca++, and creatinine clearance also were unchanged. An 8-hour infusion of parathyroid hormone (PTH), 10U/kg, increased mean urinary cyclic AMP from 5.72 to 16.95 μM/G creatinine ($p<.01$) before and from 3.84 to 14.85 μM/G creatinine ($p<.001$) after Li. At the same time mean tubular reabsorption of phosphorus (TRP) decreased from 81.5 to 70.3 per cent ($p<.005$) before and from 83.7 to 67.0 per cent ($p<.001$) after Li treatment. These effects of PTH before and after Li treatment were not significantly different. There were also no changes in clearances of total and ionized Ca^{++}, sodium and creatinine with PTH. The present results demonstrate a significant hypocalciuric effect of Li which is independent of changes in filtered Ca^{++} load, sodium excretion or altered sensitivity to PTH. Thus, Li may directly stimulate tubular Ca^{++} reabsorption and be of value in the treatment of idiopathic hypercalciuria.

Clinical Use of Serum Thyrotropin (TSH) Radioimmunoassay: The Low Thyroid Reserve Syndrome

MAJ Robert A. Adler, MC, COL James J. Bergin, MC, and T. P. O'Barr, PhD

Patients with symptoms and signs of hypothyroidism are often found to have "normal" values of serum thyroxine or other thyroid function tests. Further study of several of these patients has revealed that many have elevated serum thyrotropin (TSH) as measured by radioimmunoassay. This suggests that the anterior pituitary is attempting to stimulate further thyroid production and that the "normal" values of serum thyroxine are not truly normal for this particular patient. This has been called the low thyroid reserve syndrome. It illustrates the fact that serum TSH is the most sensitive indicator of primary hypothyroidism. Normal patients have a serum TSH level of 5 μU/ml or less; indeed 20 per cent of normal patients have a TSH level undetectable by present methods. Hypothyroid patients have TSH levels higher than 5.0 μU/ml, and TSH can be further stimulated by the administration of exogenous thyrotropin releasing hormone (TRH). Patients with hyperthyroidism have undetectable levels of TSH. Serum TSH serves as the best measurement of replacement or suppression therapy with exogenous thyroid hormone.

Chronic Lymphocytic Thyroiditis, Thyrotoxicosis and Low Radioactive Iodine Uptake

MAJ Stephen R. Plymate, MC, COL Martin L. Nusynowitz, MC, and MAJ Franklin B. Gluck, MC

The presence of thyrotoxicosis and chronic lymphocytic thyroiditis does not necessarily indicate the supervention of Grave's disease. We have defined a group of patients with clinical and laboratory evidence of thyrotoxicosis in whom the radioactive iodine uptake was low. Thyroid biopsies on these patients show chronic lymphocytic thyroiditis without histologic evidence of Grave's disease. Thyrotoxicosis subsided spontaneously in all patients.

Thus there are at least two distinct entities in which thyrotoxicosis and chronic lymphocytic thyroiditis occur concomitantly. In the usual form, histologic features of both Grave's thyrotoxicosis and chronic lymphocytic thyroiditis are present, and the radioactive iodine uptake is elevated; specific therapy directed toward the amelioration of hyperthyroidism is required. In the type of thyrotoxicosis reported herein, the radioactive iodine uptake is low and the thyroid gland reveals only pathologic features of chronic lymphocytic thyroiditis. The thyrotoxic state is presumably due to release of stored hormone by the inflammatory process. The thyrotoxicosis in this entity subsides spontaneously, and surgical, medical, or radiation therapy is contraindicated. Studies of iodine metabolism as related to one of these patients are presented.

Endocrine Evaluation of the Testes—1975

MAJ Stephen R. Plymate, MC

"Besides, he is a drake. So it does not matter so much"—Hans Christian Anderson, "The Ugly Duckling." Unfortunately this is too often the approach towards testicular failure. It must be remembered that untreated Leydig cell failure leads to premature osteoparosis and loss of muscle mass as well as loss of self-esteem, and frustration in one's daily life. With seminiferous tubular failure, unnecessary and expensive procedures are often performed on the female because of failure to look at the male factor. Secondary testicular failure, on the other hand, may be a sign of the presence of a pituitary tumor. In this discussion the appropriate clinical use of the radioimmunoassays of gonadotropins and testosterone and the use of LH/FSH releasing hormone in clinical evaluation of hypothalamic-pituitary disease is presented. The use of some older tools, such as semen analysis, in defining the presence or absence as well as etiology of hypothalamic-pituitary-testicular axis disease also is discussed.

Involvement of the Heart and Pericardium in the Malignant Lymphomas

John E. Kurnick, MD, Christine A. Petersen, MD and William A. Robinson, MD

Sixteen patients with lymphomatous involvement of heart or pericardium are presented, eight with Hodgkin's disease and eight with non-Hodgkin's lymphoma. Thirteen had Stage IV disease at the time of initial diagnosis. Cardiac involvement is usually a late manifestation of lymphoma with median onset 20 months after initial diagnosis. Fourteen patients received radiotherapy or chemotherapy prior to the onset of cardiac disease. All patients had radiologic evidence of pulmonary, pleural, or mediastinal involvement. Cardiac or pericardial disease in six was apparently due to direct extension of other intrathoracic tumor masses. Cardiac involvement was diagnosed ante-mortem in only six, although retrospectively an additional four had objective clinical evidence of cardiac involvement.

Three patients are alive without evidence of disease 20, 25, and 62 months after tissue diagnosis. Three patients whose hemodynamically significant pericardial effusions were treated medically died from non-cardiac causes with resolution of pericardial effusions prior to death. Since cardiac lymphomas may respond to therapy with prolonged survival, it is imperative that clinicians suspect cardiac or pericardial involvement in lymphoma patients who have radiographic evidence of intrathoracic lesions (especially adjacent to cardiac borders), unexplained tachyarrhythmia or conduction disturbance, evidence of outflow obstruction, or signs and symptoms suggesting pericardial effusion or tamponade.

The Treatment of Diabetic Ketoacidosis and Severe Hyperglycemic States Using Intravenous Low-Dose Insulin Therapy

Robert G. Bosworth, Jr, MD, and Terry Haney, MD

A departure from traditional treatment of diabetic ketoacidosis is represented by intravenous slow infusion of insulin in surprisingly low doses. The principles of electrolyte and fluid replacement are not abandoned in this approach to ketoacidosis therapy, but there seem to be many advantages as well as some disadvantages. So called "low dose insulin therapy" involves amounts of approximately 0.1 unit per kilogram of body weight per hour. Different variations on this concept as well as supporting background information from the literature are presented in highlight form. Two or three brief examples are given from our current series of eight cases treated in the private urban hospital, including acute medical-surgical complications during the course of acute ketoacidosis.

Crohn's Disease Developing in a Marital Partner

P. B. Miner, MD, and I. E. Vinnik, MD

Familial studies of patients with Crohn's disease have suggested a genetic predisposition requiring an environmental factor for clinical expression. This report describes the previously unreported occurrence of Crohn's disease beginning in the spouse after twelve years of marriage. The possible significance of this observation is discussed. Although the occurrence of Crohn's disease in this married couple could be due to chance, it is consistent with the hypothesis of a transmissible environmental agent as the cause of Crohn's disease.

Fever of Unknown Origin: Update

Martin J. Rubinowitz, MD

Although fever of unknown origin is a subject which is intriguing to most physicians, there are relatively few papers about this fascinating subject. Since Peterdorf and Beeson's classic article in 1961, an increasing number of diagnostic tools have become available to the clinician. Helpful blood tests include the RA test, LE prep, ANA, CEA, GGTP, and iso-enzymes of alkaline phosphatase, LDH, and CPK. Radiographic procedures that are useful diagnostically include lymphangiography, renal and hepatic arteriography, abdominal ultrasound, and lung, liver, and bone scans. Panendoscopy, with or without cholangio-pancreatography and colonoscopy, may provide answers. Surgical procedures, including temporal artery biopsy, mediastinoscopy, and liver biopsy, especially via peritoneoscopy, may spare the patient a laparotomy. The indications for and the yield from exploratory laparotomy are discussed.

By utilizing these new procedures in a thoughtful systematic way, the clinician can establish the diagnosis with the least morbidity possible, thus maximizing the chances for successful treatment.

Transbronchial Lung Biopsy via Fiberoptic Bronchoscope in Sarcoidosis

MAJ Clyde H. Koontz, MC, MAJ Lee Roy Joyner, MC and COL Roald A. Nelson, MC

In evaluating the patient suspected of having sarcoidosis, tissue conformation of diagnosis is frequently desired. The technics of open thoracotomy and mediastinoscopy have become increasingly refined over the last two decades and will demonstrate non-caseating granulomas in lung tissue and hilar lymph nodes, respectively, in nearly all cases of thoracic sarcoidosis. However, this high diagnostic yield carries the price of some significant morbidity and even occasional mortality. Search for another reliable, safe, low morbidity diagnostic procedure is warranted.

In a prospective study at two medical centers, forty-two consecutive patients suspected of having thoracic sarcoidosis without prior tissue confirmation underwent transbronchial lung biopsy (TBB) via the flexible fiberoptic bronchoscope. TBB was positive (noncaseating granulomas demonstrated in lung and/or bronchial tissue) in twenty-three of the thirty-eight cases (61%) in which adequate tissue was obtained. Special stains and cultures for acid-fast bacilli and fungi were negative in these cases and sarcoidosis was subsequently diagnosed in all patients in this series. Positive TBB was obtained in eleven of twenty cases (55%) with radiographic stage I disease, ten of fifteen cases (67%) with stage II disease, and in two of three cases with stage III disease. There was a higher probability of a positive TBB in patients with higher symptom scores for cough, wheezing, and dyspnea, and in those with a significantly restricted forced vital capacity.

There were no significant complications from the procedure. We believe that TBB via the flexible fiberoptic bronchoscope is a simple, safe, attractive initial procedure in suspected cases of sarcoidosis where tissue confirmation is desired, with advantages over liver biopsy, mediastinoscopy, and open lung biopsy.

The Clinical Spectrum of Histoplasmosis

MAJ Vernon J. Nessan, MC

The spectrum of histoplasmosis presents a widely varied clinical, roentgenographic, and therapeutic picture. Experience at Fitzsimons Army Medical Center is reviewed with roentgenographic presentations of acute primary, disseminated, and chronic cavitary histoplasmosis. The clinical presentation and therapy for each entity is discussed. Residuals of acute infection (histoplasmoma, broncholithiasis, fibrosing mediastinitis) are discussed via their roentgenographic presentation.

The Outpatient Treatment of Refractory Hypertension with Minoxidil

MAJ John P. Kleiner, MC, LTC John H. Ball, MC, and COL William P. Nelson, MC

Minoxidil is a new potent oral antihypertensive agent which is effective in the treatment of severe refractory hypertension. We studied Minoxidil in eleven outpatients with hypertension uncontrolled by aggressive treatment with standard antihypertensive agents. Ages ranged from 20 to 51, six were male, five were female, and treatment duration varied from 1 to 12 months with a mean of 6 months. The hypertension was essential in six, renovascular in two, and secondary to miscellaneous primary renal disease in three. Two patients required maintenance hemodialysis. All eleven were outpatients. The patients were instructed on a 2-3 gm salt restricted diet. Propranolol and furosemide were added as needed to control fluid retention and reflex tachycardia.

Minoxidil was highly effective in all patients. Blood pressure was decreased from a mean of 181/118 to 134/85. Nine patients developed significant peripheral edema at least once during treatment, and one patient required admission for congestive heart failure. Fluid retention was controlled with diuretic treatment in all patients and in no case required discontinuance of the drug. Four patients complained of symptomatic tachycardia which was easily controlled with propranolol. All patients developed hirsutism, but this was a major problem only in the five female patients. Four of five women were controlled with depilatory agents, but in a fifth, hirsutism necessitated discontinuance of the drug. No patients experienced orthostatic hypotension, and none had significant electrocardiographic changes. Four male patients, previously impotent on other antihypertensive medications, enjoyed a return of sexual function on Minoxidil.

We conclude that Minoxidil is an extremely effective oral antihypertensive agent in the outpatient management of severe refractory hypertension. The side-effects which include fluid retention, hirsutism, and reflex tachycardia require close observation during the intial phase of treatment, but are readily controlled.

The Hyperpnea of Exercise

G. F. Filley, MD

New data on the problem of the normal stimulus to increase ventilation with exercise point to the importance of intrapulmonary (post capillary) chemoreceptors sensitive to plasma pH changes occurring while blood is in the lungs. Because of the absence of carbonic anhydrase in the plasma, extracellular dehydration of carbonic acid cannot keep pace with CO_2 unloading from the red cells. The resulting acidification of plasma is intensified by three processes all known to occur at the onset of exercise: increased venous return, CO_2 loading of venous blood, and hyperventilation.

Plasma acidification is retarded or even stopped by certain types of CO_2 breathing because CO_2 when added to the airways (rather than to the mixed venous blood) "clogs" the control machinery. Carbon dioxide can be a ventilatory depressant rather than a stimulant. Non-invasive tests applicable to exercising patients can elucidate the control of ventilation and perhaps clarify the problem of dyspnea as well as exercise hyperpnea.

Psuedo Infarction Patterns

LTC Troy H. Williams, MC

Abnormal Q-waves with associated ST segment and T-wave abnormalities are the diagnostic electrocardiographic features of myocardial infarction. Because similar electrocardiographic features or pseudo infarction patterns may be produced by other clinical conditions, caution is necessary in diagnosis of myocardial infarction by electrocardiographic changes alone. Because of the social and economic implications of diagnosis of infarction, it is important for the clinician to be aware of these many electrocardiographic variables.

Recognized conditions or abnormalities simulating infarction include (1) normal variants, especially in young athletic individuals, (2) physiologic stimuli, especially exercise and hyperventilation, (3) ventricular hypertrophy, (4) pulmonary disease, including chronic obstructive pulmonary disease and acute pulmonary embolism, (5) myocardial diseases, primary and secondary, (6) conduction abnormalities, left bundle branch block, left anterior hemiblock, Wolff-Parkinson-White syndromes, (7) neurologic diseases, intracranial hemorrhages, muscular dystrophy, and (8) congenital defects, Ebstein's anomaly, corrected transposition of the great vessels. The electrocardiographic abnormalities produced can usually be explained by understanding of the conduction pathways, altered routes of depolarization, cardiac positions, and hypertrophy patterns. The normal variants or changes induced by various stimuli can frequently be normalized by various physiologic and pharmacologic maneuvers. Review and electrocardiographic demonstration of these various conditions simulating infarction patterns are presented, with discussion of the physiologic or pathologic mode of their production.

Evaluation of Saphenous Vein Bypass Surgery Using Multistage Treadmill Test and Ventricular Function Correlated with Graft Patency

MAJ Robert F. Bode, Jr, MC

Previous studies have indicated symptomatic improvement or relief of angina and improved exercise tolerance following saphenous vein graft surgery. Graft patency and ventricular function have been correlated with improved exercise performance. This study is designed to examine the experience with patients suffering from chronic stable angina, who have undergone saphenous vein graft surgery. Attention is directed at postoperative results of multistage treadmill testing, graft patency rate, and ventricular function as parameters of improved myocardial oxygen delivery. Comparisons are made between patients with complete revascularization and patients with postoperative residual ischemia due to graft failure, progressive disease, or lesions which were not surgically correctable. The data examines pre and postoperative submaximal exercise test results, frequency of stress induced angina and ST segment changes, as well as postoperative graft patency and ventricular function as indicated by left ventricular stroke work index and ejection fraction.

The Exercise Electrocardiogram

Thomas A. Huffman, MD

The popularity of exercise electrocardiography has increased greatly in recent years but its diagnostic value in detecting asymptomatic coronary artery disease remains uncertain. Three hundred seventeen predominantly middle-aged white male executives have undergone 0.85 submaximal, graded, multi-stage treadmill exercise studies over the past two and a half years at the Mountain Bell Medical Department. The majority have had at least two such tests, as part of the annual executive periodic examination, and an average of four prior double Master 2-step tests. Only eight subjects had positive tests (2.5%) of whom four were coronary suspects, two had probable prior myocardial infarction, and only two had a negative history. There were fourteen (4%) subjects with nondiagnostic abnormalities of whom five had negative subsequent treadmill tests and two later sustained an acute infarction. There were three false negative studies, and there was one false positive which was apparently related to "Glucola" ingestion. Prior Master's studies were in general unrevealing, largely due to inadequate heart rates, with only two positive tests in eight previous years.

We, therefore, did not find submaximal treadmill exercising of much value as a diagnostic tool. However, we hope to be able to use it as an introduction to physical fitness programs in the future.

Myocardial Infarct Imaging With Technetium Pyrophosphate

Frederick R. Gydesen, MD, and Thomas A. Verdon, MD

The development of technetium ^{99m}pyrophosphate as a myocardial infarction imaging agent now permits for the first time a visual representation of the actual size of an acute myocardial infarction. After the administration of 15 millicuries of this isotope, anterior, lateral and left anterior oblique scans of the myocardium will reveal the presence of infarcted myocardial tissue within 30 to 45 minutes post injection. Assessment of size of myocardial infarction may be of help for prognostic value. This tool also offers the clinician another way of detecting myocardial infarctions particularly in patients whose EKG has been distorted by left bundle branch block or old previous myocardial infarctions. The scan diagnosis can be made in a short time frame which offers an advantage over the more time consuming enzyme methods.

We have studied 150 patients admitted with the diagnosis of possible acute myocardial infarction. Myocardial scans were obtained from one to five days following the onset of chest pain. In fifteen patients with documented acute transmural myocardial infarction, the myocardial scan localized the area of infarction. Thirteen patients with proven acute subendocardial myocardial infarction were scanned and demonstrated agreement with the diagnosis in all cases. Thirty-six patients not substantiated by conventional laboratory methods to have had myocardial infarction were scanned and found to be normal in thirty-four instances.

The acute myocardial infarction scan has been proven to be reliable and agree with other conventional means of diagnosis. The study offers new opportunities for evaluation of acute myocardial infarction by determining the extent of involvement by infarction and by demonstrating myocardial infarction when the electrocardiogram has been distorted by previous disease.

Myocardial Profusion Scanning Correlated With Coronary Arteriography

Fred W. Schoonmaker, MD, N. K. Vijay, MD,
Donald Fink, MD, and Barbara Matthews

To determine the accuracy, viability, and profusion of the myocardium, microaggregates of labeled albumin have been directly injected into each right and left coronary artery. The microaggregates are albumin labeled with ^{99m}Tc and ^{131}I with the dose range from 300-800 thousand particles with 0.1 to 0.3 mg. of albumin.

Coronary arteriography is an established procedure which can demonstrate the anatomical circulation within the coronary arterial system. At present, there is no good technic to evaluate the actual flow or profusion of the smaller vascular beds and/or to predict the state of profusion of the myocardium at the capillary or pre-capillary level. This scanning technic has been used in normal, abnormal, and bypass graft arteries to determine the profusion of the distal myocardial segments. Scanning and angiographic correlation has been done to determine the reliability and profusion of the myocardial segments, and the presence or absence of arterial disease.

The correlation between angiography and profusion scanning adds to the overall evaluation of a coronary study.

Myocardial Imaging in Coronary Disease

Joseph Snyder, MD, Clarke C. Godfrey II, MD and
Wayne Wenzel, MD

Myocardial imaging studies have been performed in approximately 175 patients with and without obstructive coronary disease at the time of angiography. Macroaggagates of albumin labeled with ^{131}I and ^{99m}Tc were injected into the coronary arteries. Studies were also performed in patients suspected of having acute myocardial infarction by intravenous injection of ^{99m}Tc stannous pyrophosphate.

Scintigrams obtained at the time of angiography have been used as an aide in selecting patients who might benefit from myocardial revascularization, as angiography may not always predict the status of myocardial perfusion. If perfusion is absent or markedly impaired surgical benefit is unlikely. Perfusion studies have been found to be of value in ventricular aneurysms and cardiomyopathies.

Scintigrams obtained in suspected myocardial infarction may be of value in (1) following coronary artery bypass surgery, (2) underlying bundle branch block, (3) ST and T wave changes without enzyme changes, (4) previous transmural myocardial infarction with extension, and (5) serum enzyme elevation without Q waves. Reasons for false positive and false negative scintigrams are discussed.

Coagulation Factors Influencing Thrombosis of Aorto-Coronary Bypass Grafts

COL J. J. Bergin, MC, LTC R. Zajtchuk, MC,
LTC G. F. Schuchmann, MC, COL W. H. Heydorn, MC,
and COL T. E. Strevey, MC

Unsatisfactory technic or severely diseased distal coronay arteries are usually blamed for early occlusion of aorto-coronary bypass grafts. This study is a retrospective evaluation for hypercoagulability of thirty patients who had occlusion of aorto-coronary vein grafts within one year of surgery. Blood flows through the graft, measured at operation, ranged between 35 and 90 cc. per minute. Five patients had documented pulmonary emboli within 30 days of the operation. The following parameters were studied: generation of thrombin, antithrombin-III level, activated partial thromboplastin time, factor VIII assays, fibrinogen levels, platelet count and platelet adhesiveness. Twenty-three of the thirty patients were found to be hypercoagulable, as evidenced by low antithrombin-III, high thrombin generation index or high factor VIII values. Three patients had abnormal platelet adhesiveness. All patients who had pulmonary emboli were found to be hypercoagulable.

These data suggest that thrombin generation, serum antithrombin-III and factor VIII determination may identify patients predisposed to pulmonary embolism and premature closure of the aorto-coronary bypass grafts. A prospective study is in progress to determine if discrimination of the hypercoagulable patient and, thus, anticoagulation intervention is feasible.

Signs, Symptoms and Risk Factors of Coronary Heart Disease in Patients Having Coronary Arteriography

LTC Bruce H. Brundage, MC, Roger L. Simmons, MD, and
William P. Nelson, MD

All patients having coronary arteriography at Fitzsimons Army Medical Center during the past three years had historical physical examinations and laboratory data recorded at the time of angiography. This information, along with coronary artery anatomy, was stored in a computer at St. Luke's Hospital, Denver. There have been 322 patients incorporated into the study. It is now possible to make multiple cross-correlations with regard to signs, symptoms, and risk factors of coronary heart disease and extent and types of coronary artery obstruction. The incidence of major and minor complications of coronary arteriography was also recorded and reflects the current risk for this procedure.

Abstracts which are not to be presented at the Joint Meeting are continued on page 539.

MEETINGS

CONTINUING EDUCATION IN PATHOGENESIS AND TREATMENT OF HEADACHE

Albuquerque Hilton Inn,
Albuquerque, New Mexico

January 8-10, 1976

Contact: Otto Appenzeller, MD, PhD, 1007 Stanford Drive, NE, Albuquerque, New Mexico 87131.

American College of Cardiology
Santa Barbara Heart and Lung Institute

FUTURE DIRECTIONS IN THE MANAGEMENT OF CARDIAC DISEASE— A BICENTENNIAL VIEWPOINT

Snowmass-at-Aspen, Aspen, Colorado

January 11-13, 1976

Contact: William D. Nelligan, American College of Cardiology, 9650 Rockville Pike, Bethesda, Maryland, 20014.

University of Oklahoma Department of Medicine—
National Academy of Medicine of Mexico

INTER-AMERICAN SYMPOSIUM OF INTERNAL MEDICINE

Centro Medico Nacional, Instituto Mexicano
Del Seguro Social, Mexico City, Mexico

January 12-15, 1976

Contact: James F. Hammarsten, MD, University of Oklahoma Health Sciences Center, P.O. Box 26901, Oklahoma City, Oklahoma 73190.

American College of Emergency Physicians-
Emergency Department Nurses Association

SECOND ANNUAL ROCKY MOUNTAIN REGIONAL CONFERENCE ON EMERGENCY MEDICINE AND NURSING

January 14-17, 1976

Keystone Lodge, Keystone, Colorado

Contact: Ellen H. Taliaferro, MD, St. Joseph Hospital, 1835 Franklin Street, Denver, Colorado 80218.

American College of Physicians

COLORADO REGIONAL MEETING

January 15-17, 1976

The Broadmoor, Colorado Springs, Colorado

Contact: Robert V. Elliott, MD, St. Luke's Hospital, 601 East 19th Avenue, Denver, Colorado 80203.

Albuquerque and Bernalillo County
Medical Association

VAIL MEDICAL-SKI SYMPOSIUM—CARDIOLOGY FOR THE NON-CARDIOLOGIST

January 16-17, 1976

Contact: David R. Holten, MD, 8401 Constitution, NE, Albuquerque, New Mexico 87110.

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TAOS MEDICAL-SKI SYMPOSIUM

February 18-21, 1976

Contact: Thomas A. Bodnar, 2650 Yale Blvd., SE, Suite 103, Albuquerque, New Mexico 87106

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PURGATORY MEDICAL-SKI SYMPOSIUM—HYPERTENSION 1976

Durango, Colorado

March 12-13, 1976

Contact: David R. Holten, MD, 8401 Constitution, NE, Albuquerque, New Mexico 87110.

Lovelace Foundation

CURRENT CARDIOVASCULAR PROBLEMS

Lovelace-Bataan Medical Center

January 16-17, 1976

Contact: Martin J. Conway, MD, Lovelace Foundation, 5200 Gibson Blvd., SE, Albuquerque, New Mexico 87108.

The American Medical Center
at Denver

CANCER CHEMOTHERAPY COMMUNICATIONS CARE, SERIES I

January 19-30, 1976
June 21-25, 1976

The American Medical Center
at Denver,
6401 West Colfax Avenue,
Denver, Colorado 80214

Contact: Dorothy E. Howard, RN, American Medical Center.

University of Colorado School of Medicine,
Continuing Medical Education

FAMILY PRACTICE REVIEW

January 19-24, 1976

Humphreys Postgraduate Center,
University of Colorado Medical Center,
4200 East 9th Avenue,
Denver, Colorado

* * *

THROMBOSIS: CURRENT CONCEPTS OF, DIAGNOSIS, & TREATMENT

February 2-4, 1976

Given Institute of Pathobiology,
Aspen, Colorado

Contact: Office of Postgraduate Medical Education, 4200 East 9th Avenue, Denver, Colorado 80220.

Rocky Mountain Academy of
Occupational Medicine

ELEVENTH ANNUAL INSTITUTE OF INDUSTRIAL MEDICINE

January 22-23, 1976

The Broadmoor,
Colorado Springs, Colorado

Contact: W. Lloyd Wright, MD, Coors Medical Center, Golden, Colorado 80401.

Colorado Heart Association

HIGH COUNTRY CARDIAC CONFERENCE

January 22-24, 1976

Crossroads Cinema Theatre, Vail, Colorado

Credit: 12 hours Continuing Medical Education.
Contact: Colorado Heart Association, 4521 East Virginia Avenue, Denver, Colorado 80222.

American College of Physicians—

Stanford University Medical Center

POSTGRADUATE COURSE ON INFECTIOUS DISEASE

January 26-30, 1976

Keystone Lodge, Keystone, Colorado

Contact: Jack S. Remington, MD, 300 Homer Street, Palo Alto, California 94301.

Montana Medical Association

BIG MOUNTAIN MEDICAL-SKI CONFERENCE 18TH ANNUAL SESSION

January 27-30, 1976

The Big Mountain, Whitefish, Montana

Contact: R. D. Buchanan, MD, P.O. Box 220, Columbia Falls, Montana 59912.

American Cancer Society,
Colorado Division

MIDWINTER CANCER SEMINAR

January 28-30, 1976

Vail Village Inn, Vail, Colorado

Contact: American Cancer Society, 1809 East 18th Avenue, Denver, 80218.

U. S. Virgin Islands Medical Society

MID-WINTER VIRGIN ISLANDS CLINICAL CONFERENCE

January 29-31, 1976

Contact: U. S. Virgin Islands Medical Society, P. O. Box 1442, Charlotte Amalie, St. Thomas, U. S. Virgin Islands 00801 (Via AIRMAIL)

Colorado Trudeau Society

15TH J.R. DURRANCE
MID-WINTER CHEST CONFERENCE

February 1-4, 1976

Aspen Institute of Humanistic Studies,

Aspen, Colorado

Contact: Ronald D. Engler, Colorado Trudeau Society, 1600 Race Street, Denver, Colorado 80206.

University of New Mexico
School of Medicine

2ND ANNUAL ROCKY MOUNTAIN NEURO-OPHTHALMOLOGY COURSE

February 5-7, 1976

Santa Fe Hilton,
Santa Fe, New Mexico

Contact: Thomas J. Carlow, MD, c/o Neuro-Ophthalmology Course, Department of Neurology, University of New Mexico School of Medicine, 1007 Stanford Drive, NE, Albuquerque, New Mexico 87106.

Continued from Page 536

The Abnormal Sella Turcica—A Tumor Board Review

LTC Fred D. Hofeldt, MC and John E. Kurnick, MD

An eighteen year review of the Fitzsimons Army Medical Center Tumor Board disclosed 146 patients with intracranial neoplasms or arterial aneurysms. Sixty of these had roentgenographic abnormalities of the sella turcica and form the basis of this study. These abnormalities of the sella are most commonly due to chromophobe adenoma (30), craniopharygioma (10), and acromegaly (7), but a surprisingly large number of abnormalities were caused by lesions arising distant to the sella (10). There were three cases of empty sella syndrome. Headache, visual disturbance, and sexual dysfunction were the most frequent presenting complaints, and visual field abnormality was the most common physical finding. Pituitary dysfunction was manifested most frequently by alterations in growth hormone and gonadotrophin secretion and less frequently by hypothyroidism and adrenocortical insufficiency. When the abnormal sella was associated with evidence of symptomatic intracranial disease, endocrine dysfunction, or visual field compromise as evidence of an anatomically aggressive neoplasm, specialized neuroradiographic localizing procedures were usually positive, and treatment for most of the causative lesions was highly effective. A systematic approach to the evaluation and therapy of patients with radiographic abnormalities of the sella turcica based upon the aggressivity of the responsible lesion is developed.

Four-Hour Thyroid Scan With I-123

Stewart L. Rosenthal, MD, Thomas A. Verdon, Jr., MD, and Frederick R. Gydesen, MD

The majority of patients seen in the Nuclear Medicine Clinic for thyroid evaluation have been referred for the elucidation of structural abnormalities, most often goiter or nodules. Until recently the usual method of evaluating these patients was to administer a normal dose of I-131 and have them return the next day for a rectilinear thyroid scan. The 24-hour interval between dosing and scanning is inconvenient for the patient, particularly those who work and those who must come to the hospital from distant points.

Because of the ideal physical characteristics of I-123 it is now possible to administer a larger dose of this radionuclide than that of I-131. In spite of the increased dose the patient still receives approximately 100 fold less radiation than the conventional I-131 scanning dose. Because of the increased count rate obtained it is now possible to perform scans at 4 hours post dosage and have a true representation of both organic trapping and organification of iodine by the thyroid gland. This permits accurate scan diagnosis of the structural thyroid abnormalities. Thyroid scans were performed 4 and 24 hours after the administration of I-123 solution in 124 patients. The 4-hour scans and 24-hour scans were found to be of equal diagnostic value. Therefore, in individuals with structural thyroid abnormalities the time required for scan evaluation may be reduced to 4 hours.

Prolactin Response to Water Loading in Hypothyroidism

MAJ Stephen R. Plymate, MC, MAJ Franklin B.Gluck, MC and COL Martin L. Nusynowitz, MC

The serum prolactin response to water loading has been proposed as a means of differentiating patients with galactorrhea due to pituitary tumors from those with functional galactorrhea. This response was studied in six patients with primary hypothyroidism. In contrast to patients with functional galactorrhea alone, the hypothyroid patients did not manifest suppression of serum prolactin with water loading. Four patients showed a significant rise and two patients showed no change in their prolactin response. The hypothyroid state appears to result in an augmentation of prolactin release possibly because in the hypothyroid state there is impaired excretion of free water and decreased serum osmolality with water loading. The rise in prolactin may be a mechanism for maintaining plasma osmolality. In addition, the water loading test in hypothyroidism is not a consistently reliable test in discriminating presence or absence of pituitary tumor causing galactorrhea.

Continuous Insulin Infusion for the Treatment of Diabetic Ketoacidosis

MAJ Robert A. Adler, MC, LTC Fred D. Hofeldt, MC, MAJ Needham Ward, MC, and T. P. O'Barr, PhD

In the recent past, diabetic ketoacidosis has been treated with intravenous bolus doses of 100 to 200 units of insulin every 2 to 4 hours. However, it has now been found that constant infusion of smaller doses is advantageous. After a loading dose of 10 to 20 units intravenously, an infusion of saline, albumin, and insulin delivers 0.1 unit of insulin per kilogram per hour to the patient. This has resulted in a smooth decrease in glucose and ketones with the distinct advantage that the insulin can be stopped instantaneously if blood sugar falls precipitously. Serum insulin levels of greater than 40 μU/ml have been measured in new diabetics given this treatment. Serum glucose tends to decrease sooner than ketones as measured by nitroprusside reaction. Therefore, when the blood sugar reaches 250 mg/100 ml, the insulin infusion rate is decresed and intravenous glucose is begun. Ten patients have been treated with this regimen with excellent results and no mortality.

Coronary Arteriography by Single Catheter Percutaneous Femoral Technic: Experience in 7,200 Cases

F. W. Schoonmaker, MD and N. K. Vijay, MD

A new percutaneous femoral method for studying the coronary arteries, left ventricle, and saphenous vein bypass grafts using a single catheter has been developed. A #8 French 100 cm polyurethane catheter with wire incorporated with a 45° curved tip has been used in 7,200 patients. This technic combines the speed and simplicity of the percutaneous femoral approach with the safety of the single catheter technic by eliminating multiple catheter and guidewire changes. Manipulation technics for selective right and left coronary artery and saphenous vein bypass injections as well as for left ventriculography will be shown in a film clip. In less than 10 per cent of cases has it been necessary to change to a second catheter. Catheterization time has averaged less than 15 minutes. Complications have been infrequent: femoral thrombosis 0.3 per cent, hematoma 0.2 per cent, myocardial infarction 0.04 per cent, cerebrovascular accident 0.03 per cent, and death 0.07 per cent. We feel that the speed of the technic and the elimination of multiple catheter changes have contributed to the low complication rate.

Correlation of ST Segment in Submaximal Stress Testing and Coronary Arteriography

Fred W. Schoonmaker, MD, N. K. Vijay, MD and
Jeanne E. Day, RN, MS.

In order to evaluate the correlation between ST segment depression in submaximal stress treadmill and coronary artery disease by coronary arteriography, 1,574 patients were studied. Patients on cardiac medications or with electrolyte imbalance and known heart disease were excluded. Simultaneous 3-lead, V4, V5, and V6 system was used with positivity or negativity being 1 mm depression of the ST segment and .08 second duration in three successive beats and 85 per cent predicted capacity by heart rate achieved.

In 1,045 males, there were 55 (5%) false positives and 148 (14%) false negatives. In a total of 529 females, there were 86 (16%) false positives and 12% false negatives. Sensitivity (true/total positive) is .70 while specificity (true/total negative) is .80.

These data indicate that there is a good correlation between sensitivity and specificity of stress testing and the presence or absence of coronary artery disease by arteriography.

Coronary Serialography with 105mm Camera

F. W. Schoonmaker, MD, N. K. Vijay, MD and
Jerry S. Rich, BS.

In order to evaluate the 105mm camera, correlations have been made with 35mm cine for image detail. (1) Procedurally the camera is used as a 35mm with simultaneous fluoroscopy, "panning", and tape review. (2) Technically, film mat is 95X 100mm, cine is 18X 24mm; frame rate capacity is ½-12/sec. and 7.5-150/sec. for cine. (3) System resolving power is 1 LP/mm (6") and 2 LP/mm (6") for 35mm; anatomical field sizes may vary with both from 6.5" diameter to 3.4" and the focal spot size of .6-1mm; peak mA is 800 for 105mm and 300-400 for 35mm and longer exposure times; KV_p range is approximately the same. (4) Radiation requirements are 100 mR with the 105mm and 200 mR with cine, giving a cumulative exposure per second at indicated frame rate, .4 mR at 4 frames/sec. as compared to 1.2 mR at 60 frames/sec. (5) Image resolution is 3 LP/mm compared to 2 LP/mm with a transillumination system, not optical.

These comparisons show that this photofluorographic technic increases diagnostic image detail and resolution.

Resting ST Depression in the Standard Scalar Electrogradiogram Correlated with Coronary Angiograms

F. W. Schoonmaker, MD, N. K. Vijay, MD and
Jeanne E. Day, RN, MS.

In order to determine the correlation between the resting scalar electrocardiogram (EKG) and the presence or absence of coronary artery disease (CAD), 1,574 patients were evaluated by EKG and coronary arteriography (C.A.). The standard used was primary ST (PST) segment of .10 MV or more negative in any three complexes of any lead except AVR with .08 second duration. Patients on cardiac medications, electrolyte imbalance, or known heart disease were excluded.

Of the 1,574 patients studied, 186 had PST changes and evidence of CAD (12%). No PST with presence of CAD was seen in 820 (53%). There were 48 (3%) with PST changes and no evidence of CAD. Patients with no PST and CAD were 493 (34%). Sensitivity (true/total positive) was 18 per cent with a specificity (true/total negative) of 63 per cent.

These data show poor correlation between the resting ST segment in the 12 lead scalar EKG and the presence or absence of angiographically demonstrated CAD.

Correlation of Exertional Premature Ventricular Contractions and Coronary Arteriography

F. W. Schoonmaker, MD, N. K. Vijay, MD and
Jeanne E. Day, RN, MS.

In order to evaluate the correlation of exertional premature venticular contractions (PVCs) and coronary artery disease (CAD), 130 patients were studied by coronary arteriography (CA) and submaximal stress treadmill tests. All patients on cardiac medication, with electrolyte imbalance and known heart disease were excluded.

PVCs when associated with a depressed or ischemic heart are considered significant because of the vulnerability of the T wave. Of the 130 patients with PVCs studied, 101 (78%) had a definite increase in PVCs on treadmill testing and showed CAD. The most common lesions found were in main stem left, right or anterior descending artery. There were 9 (7%) false positives (no CAD with increased PVCs).

These data indicate that there is a high correlation of exertional PVCs and angiographically demonstrated CAD.

Direct Venous and Arterial Revascularization Surgery

F. W. Schoonmaker, MD, John B. Grow, Sr, MD, A. E. Prevedel,
MD, D. Young, MD and N. K. Vijay, MD.

In order to evaluate patency, clinical symptoms and left ventricular functions, 412 patients of 2,328 bypass surgical patients have been restudied. The longest followup is 7½ years. In ten per cent (43 patients) one graft was occluded, five per cent (21) had more than one graft occluded, and all grafts were occluded in six per cent (25). Sixty-one direct internal mammary grafts are included with 10 restudied and no grafts occluded.

If one or more grafts were patent, 78 per cent of the patients had no clinical symptoms with 21 per cent having improvement of symptoms. If all grafts were not patent, there was no change or worsening of symptoms. Fifty consecutive patients showed improvement of ejection fraction in 68 per cent (34), with minimal change in 12 per cent (6), and no change in 20 per cent (10). Exercise stress testing has shown "normalization" in 76 per cent, borderline result in 14 per cent, and remaining abnormal test in 11 per cent of patients with patent grafts.

These data show high incidence of patency of grafts after long duration with improvement of ventricular function and stress testing with patency.

Clinical Evaluation of Computerized Electrocardiograms in a Community Hospital

Karl H. Shipman, MD, Richard Hamilton, MD, Joseph
Snyder, MD and Robert M. Marshall, MD

A prospective study was performed to assess the degree of agreement between computer interpreted ECG's and electrocardiographer in a community hospital. Results indicated that no change was required in 44.2 per cent, a minor change occurred in 25.6 per cent, and a significant difference occurred in 30.1 per cent. Further study revealed complete agreement in 65.9 per cent of all "normal" ECG's. Of the "abnormal" ECG group, complete agreement was present in 25.5 per cent, partial agreement in 63.9 per cent and total disagreement in 10.4 per cent. These findings are compared to previous studies in the literature. Implications regarding the role of computerized electrocardiography are discussed.

Therapy in Arteriosclerotic Heart Disease—Prevention and Restoration

MAJ James E. Farr, MC

The experience in the care of the post-myocardial patient from hospital admission through return to normal activities and employment is reviewed. Inpatient cardiac rehabilitation with a followup physical conditioning outpatient program is emphasized.

Pursuit of Optimal Recovery After Myocardial Infarction and Vein Bypass Surgery

L. L. Brock, MD

The staggering prevalence and monumental economic input into coronary care and vein bypass surgery warrant all efforts be made to provide an optimal result. Research and experience has shown a consistent loss of function attending bedrest, and that carefully prescribed and supervised reconditioning is safe and effective in overcoming this loss. Loss of confidence is also a remedial component of the suboptimal recovery of most infarct patients. Loss of confidence and loss of function feed on each other unless early and effective intervention is provided.

Description and experiences of the five-year comprehensive community rehabilitation program of the Colorado Heart Association are provided. Economics and designs of this type of service in Colorado communities of different sizes are described, and interaction of services with attending physicians, family, other community agencies, employers is discussed.

Challenges With Aspirin, F D and C Dyes, and Preservatives in Asthma

MAJ Melvin Hoffman, MC

This study is to identify commonly used food dyes and preservatives which may provoke asthma. Twenty subjects were selected for challenge with aspirin, the dyes tartrazine, sunset yellow, amaranth, poinceau, indigotine, brilliant blue, erythrosine, and the preservatives sodium benzoate, parahydroxybenzoic acid, butylatedhydroxytoluene, and butylatedhydroxyanisol. Criteria for a positive challenge was a 25 per cent fall in FEV_1 reproduced in one or more series of rigorously controlled double blind challenges. Seven of nineteen subjects reacted to aspirin and an eighth developed urticaria alone. No subject reacted to tartrazine, amaranth, poinceau, sunset yellow, indigotine, brilliant blue, BHT or BHA. One clearly reacted to the preservatives sodium benzoate and parahydroxybenzoic and another reacted to erythrosine.

It is concluded that a history of aspirin idiosyncrasy in asthmatics is not reliable in predicting which patients are truly intolerant. Conclusions drawn from open testing, or a single set of challenges, whether single or double blind, may not be valid.

Double Blind Comparison of Oral Ephedrine and Albuterol in Bronchial Asthma

LTC Dudley A. Raine, Jr, MC

In a double blind study the pulmonary, metabolic, and cardiovascular responses were measured in nineteen patients while they were receiving either 4 mg Albuterol qid, 6 mg Albuterol qid, or 25 mg Ephedrine qid for a period of 12 weeks. The study was designed to answer two questions: (1) whether Albuterol in the dose employed was a better bronchodilator than Ephedrine, and (2) whether the bronchodilator response to Albuterol or Ephedrine diminished with chronic administration.

Seven patients received Ephedrine, seven patients 4 mg Albuterol, and four patients 6 mg Albuterol. There was no statistical difference between the bronchodilator responses to Ephedrine and Albuterol. The bronchodilator response to the initial dose of Albuterol was significantly better than the response to the same dose measured at two-week intervals throughout the study period. The response to the first dose of Ephedrine was also greater than the response to any subsequent dose measured, but the difference was not statistically significant. Further evidence of induced beta-adrenergic subsensitivity with chronic administration was found when the rise in blood glucose and lactate following a dose of medication was compared for the first, 15th and 85th days. The rise in glucose and lactate was consistently higher with the first dose than with similar doses administered after a period of chronic ingestion.

In the doses employed, Albuterol could not be shown to be a more effective bronchodilator than Ephedrine, and there was evidence with both Ephedrine and Albuterol, although statistically significant only with Albuterol, that chronic administration induced a state of decreased beta-adrenergic responsiveness manifest by both a decreased bronchodilator response and a decreased metabolic response to the drug.

Double Blind Comparison of Varying Treatment Schedules of Aerosolized Terbutaline in Bronchial Asthma

MAJ Wendell E. Petty, MC

Terbutaline is a sympathomimetic amine. Studies have established that it is an adrenergic agonist which is selective for beta-2 receptors. In part 1 of the present study, twelve patients received in a double blind fashion 7 inhalations at 20-minute intervals of terbutaline 125 micrograms, terbutaline 250 micrograms, and isoproterenol 100 micrograms. There was continued improvement in pulmonary functions with all three treatment schedules through the fourth dose. All reported side effects came after the fourth dose, and there was no evidence of cardiac stimulation with any of the treatments.

In part 2, each patient received 4 inhalations one minute apart for a total of 500 micrograms of terbutaline; in 4 doses of 125 micrograms, in 2 placebo inhalations then 2 doses of 250 micrograms, and finally in 3 placebo inhalations and then a dose of 500 micrograms. Regardless of how administered, 500 micrograms of terbutaline produced significant improvement in pulmonary functions in all patients, maximal by 5 minutes and maintaining effect through four hours.

Chronic Renal Disease in the American Indian

LTC John H. Ball, MC, William Bethea, MD and LTC Donald E. Butkus, MC.

From 1971 to 1975, fourteen American Indian patients with chronic renal disease were treated at Fitzsimons Army Medical Center. Ages ranged from 18 to 65, with a mean of 41.5 years. Diagnosis was chronic glomerulonephritis in five, diabetic glomerulosclerosis in three, chronic pyelonephritis in two, Henoch-Schonlein purpura nephritis in two, and rapidly progressive glomerulonephritis in one. Peritoneal dialysis was employed in eight patients (23 dialyses), four awaiting hemodialysis, and four receiving this as their only modality of therapy. The latter four returned to their Reservations refusing further therapy. Hemodialysis was performed in ten patients, eight in preparation for renal transplantation. The duration of treatment was 2 to 18 months, with a mean of 5.3 months.

Nine of the fourteen patients are still surviving, eight with successful renal transplants, and one on long term hemodialysis. Five are deceased, all on a voluntary basis, four having been on peritoneal dialysis, one voluntarily withdrawing from hemodialysis.

Five of these fourteen patients had positive intermediate PPD's, but the remainder were either not tested or not documented. Three of these five had clinically overt tuberculosis. One patient developed peritoneal tuberculosis while receiving immunosuppressive therapy for rapidly progressive glomerulonephritis, and responded to antituberculosis therapy. A second patient died from widely disseminated tuberculosis and uremia after refusing further dialysis. A third patient had recurrent epididymitis, tracheal stenosis, and chronic pulmonary disease with a strongly positive PPD. His tuberculosis was quiescent on INH therapy.

The incidence of patients refusing dialysis therapy is higher than other populations reported in the literature. Transplantation is the preferred mode of therapy in this group because it decreases social problems resulting from translocation from the Reservations. Incidence of active tuberculosis is higher than in the remainder of our dialysis population.

Norepinephrine-Induced Acute Renal Failure (ARF): A Reversible Ischemic Model

Robert E. Cronin, MD, Abby L. McCool, Keith M. McDonald, MD and Robert W. Schrier, MD

A previously described ischemic model of unilateral ARF in the dog, intrarenal norepinephrine (NE) 75 μg/kg/min for 2 hours, was studied and found to produce a severe, irreversible functional and histologic lesion. At 8 weeks the kidney was anuric and approximately 75 per cent of renal mass was lost. This approach thus could be criticized as not providing an adequate experimental model for reversible ARF in man. Therefore additional experiments in an attempt to produce a reversible model of ARF were performed. Three weeks after unilateral nephrectomy, the same dose of NE was infused intrarenally for 40 minutes in 9 anesthetized dogs. Two animals died in uremia within 14 days; 7 animals developed nonoliguric ARF with a reversible alteration in plasma urea nitrogen (PUN), plasma creatinine (P_{Cr}), urine to plasma creatinine ratio (U/P_{Cr}), and plasma renin activity (PRA). Increased PRA was not a feature of the maintenance of the ARF. The further study of this NE-induced model and utilization of measures that modify it may provide insights into the mechanism of ischemic ARF.

Prevention of Norepinephrine-Induced Acute Renal Failure (ARF)

Robert E. Cronin, MD, Antoine de Torrente, MD, Paul D. Miller, MD, Ruth Bulger, MD and Robert W. Schrier, MD

Extracellular fluid (ECF) osmolality and volume have been proposed as determinants of prevention of ARF. Thus, the preventive effect of comparable volume expansion with isotonic saline (IS), 5% isotonic mannitol (IM) and 20% hypertonic mannitol (HM) was examined in anesthetized dogs with Norepinephrine (NE) induced ARF. Three hours after intrarenal NE (.75 μg/kg/min for 40 min) glomerular filtration rate (GFR) was 1.3±1.3 ml/min SEM in the ipsilateral kidney and 52.7±2.9 ml/min in the contralateral kidney. Studies were then performed with IS (.75 ml/kg/min), IM (.75 ml/kg/min) or HM (.2 ml/kg/min) given for 30 minutes before the NE infusion. Degree of protection at 3 hours post NE was assessed as infused GFR/contralateral GFR x 100.

The protective effects of IM and HM were not statistically different from each other. A significant correlation ($p<.001$) was observed between protection and the solute excretion rate prior to the NE insult. Proximal tubular damage was seen in all four groups by light microscopy. IM and HM prophylaxis correlated with absence of "smudging" of epithelial glomerular foot processes by scanning microscopy. Prophylaxis of NE-induced ARF correlates best with the magnitude of the osmotic diuresis rather than the degree of ECF expansion, ECF osmolality or proximal tubular damage.

The Protective and Reversal Effects of High-Dose Furosemide in Norepinephrine-Induced Acute Renal Failure (ARF)

Paul D. Miller, MD, Antoine de Torrente, MD, Robert E. Cronin, MD, Ruth Bulger, MD, Keith M. McDonald, MD and Robert W. Schrier, MD

Previous studies suggest that Furosemide (F) is either of no value or is deleterious in ARF. In the present study in anesthetized dogs the value of high-dose F (10 mg/kg + 10 mg/kg/hr IV) was examined either 30 minutes prior (protective) or immediately after (reversal) induction of NE-induced ARF (intrarenal NE at .75 μg/kg/min for 40 min). For comparison with F the effect of intrarenal acetylcholine (ACH) (20 μg/min) also was studied. In all studies urinary losses were replaced to avoid volume depletion. Protection or reversal was assessed at 3 hours post NE as infused kidney GFR/contralateral kidney GFR x 100. The study shows that, in contrast to previous results in experimental ARF, NE-induced ARF cannot only be prevented but can be partially reversed by F or ACH. The greater protection with F than ACH was not due to differences in renal blood flow (RBF) or volume status, but to a higher osmolar excretion (Cosm) present with F. Protection with F was associated with normal epithelial glomerular foot processes by transmission microscopy but proximal tubular damage persisted. High-dose F therefore may be of value in the prevention and reversal of ARF by a mechanism independent on an increased Cosm and restoration of RBF.

The Effect of Splenectomy on "Tear-Drop"Erythrocytes in Agnogenic Myeloid Metaplasia

N. J. DiBella, MD, M. N. Silverstein, MD, and H. C. Hoagland, MD

"Tear-drop" shaped erythrocytes (TD) are frequently observed in the peripheral blood of patients with myelofibrosis and myeloid metaplasia (MMM). It is not certain whether these deformed cells result primarily from the myelofibrosis or the extramedullary hematopoiesis in the spleen. In order to determine the influence of the spleen on TD's we reviewed the presplenectomy and postsplenectomy peripheral blood smears from fourteen patients with MMM. These included six females and eight males ranging in age from 44 to 76 years (median 59) at the time of splenectomy. Splenectomy was performed for a variety of reasons including massive enlargement, pain or hypersplenism. The average number of TD's per 1000 RBC's in the preoperative smears was 41 (range 15 to 112) compared with 11 in the postsplenectomy smears (range 6 to 28), only one patient failing to exhibit a decrease after splenectomy. There was no definite correlation between the number of TD's and weight of the spleen removed. Based on this four-fold decrease in the number of TD's after splenectomy, we conclude that the enlarged spleen in MMM is a significant factor in TD formation.

Coagulation Defects in Patients with Severe Alcoholic Liver Disease

MAJ K. D. Herbst, MC

Coagulation studies were performed in twenty-three patients with severe alcoholic liver disease (ALD) using the thrombin time (TT), the euglobulin clot lysis time (ECLT), fibrin split products by the tanned red cell hemagglutination inhibition immunoassay (FSP/TRCHII), the protamine sulfate paracoagulation test (PPP) and the fibrin monomer aggregation test (FMA) for dysfibrinogenemia. All patients had significant alcoholic history and had demonstrated at least one episode of hepatic decompensation. Three patients were actively bleeding at the time of study. Sixteen patients demonstrated mild prolongation of the TT. A shortened ECLT was noted in four patients. Evidence of disseminated intravascular coagulation (DIC) was noted in only one; however, this patient had documented *pseudomonas aeruginosa* septicemia and his bleeding tendency and all coagulation parameters resolved with antibiotic therapy without the use of heparin. Only one other patient had elevated FSP/TRCHII (38 μg/ml) and no other patient had a positive PPP. The FMA for dysfibrinogenemia was abnormal in 20 of 21 patients studied and was markedly abnormal in the three with active bleeding.

Clinical and laboratory evidence of DIC could not be demonstrated in patients in this study except for the one with *pseudomonas aeruginosa* septicemia. Nor could evidence of clinically significant primary fibrinolysis as measured by the ECLT and FSP/TRCHII be demonstrated. The FMA was significantly abnormal in twenty of 21 studied and suggests that an abnormal fibrinogen or early (thrombin clottable) fibrinogen degradation products may be present in these patients and may explain the mild prolongation in the TT.

Sarcoidosis—The Great Mimicker?

MAJ Michael J. Boland, MC, MAJ John Redmond, MC and MAJ Joseph D. Fitterer, MC.

Although sarcoidosis may present as one of several easily recognizable syndromes such as asymptomatic hilar adenopathy, erythema nodosum, or granulomatous hepatitis, it may also present, not rarely, in a variety of unusual passions. A recent case is particularly instructive. A 37-year-old Caucasian woman presented with bilateral pleural effusions and chest x-ray evidence of an enlarged mediastinum. On further evaluation she clinically demonstrated evidence of superior vena cava compression, and this was confirmed by cardiac catheterization and angiography. Thoracentesis obtained cloudy serosangenous fluid, and cytology was interpreted as positive for malignancy. Presumptive diagnosis of lymphoma was made, and radiation therapy was initiated. Mediastinoscopy demonstrated noncaseating granuloma and no evidence of malignancy, though the appearance of the lymph nodes to the examining surgeons was that of malignancy. Because of the lack of specific histologic diagnosis of lymphoma, the patient was subjected to open mediastinal exploration. Again, no evidence of malignancy was found, examination of the enlarged lymph nodes disclosing noncaseating granuloma. She responded clinically and radiographically to high dose prednisone therapy and, at the present time, is asymptomatic, being tapered off low dose oral prednisone. This case represents a treacherous presentation of sarcoidosis as a malignant lymphoma. Other interesting presentations will be reviewed.

Environmental Factors Associated With Urinary Tract Infections in Women

David Brandt, MD

Separation of certain environmental factors associated with urinary tract infections in women is presented. The two groups, infected and control, were selected from a community of 75,000 attending a private practice clinic. The factors selected were bathing habits and material incorporated in underclothing. All urines from both groups were examined microscopically and cultured. Methodology and results will be presented.

Treatment of Adenoma Sebaceum Lesions of Tuberous Sclerosis with Dermabrasion

MAJ Robert N. Earhart, MC, COL Donald D. Nuss, MC, MAJ Robert J. Martin, MC, MAJ Richard Imber, MC and LTC John L. Aeling, MC

Tuberous sclerosis is a congenital disorder manifested by multiple tumors of the brain, viscera, and skin. The inheritance is an autosomal dominant gene with variable expression. Seizures are common. Cutaneous lesions are common and the most significant are the adenoma sebaceum on the face. Mental deficiency is present in 60 to 70 per cent of patients and may be progressive, but if mental development has been normal throughout childhood, subsequent deterioration is uncommon. Those patients presenting with adenoma sebaceum and normal mental development may tend to be discouraged from attaining normal social integration because of disfigurement of the adenoma sebaceum lesions (angiofibromas). This paper will present two 15-year-old patients, a male and a female, with tuberous sclerosis, normal mental development and serious disfiguring lesions of adenosebaceum of the face. Both were treated with dermabrasin procedure with almost complete removal of the lesions and an excellent cosmetic result.

Epidermodysplasia Verruciformis

LTC John L. Aeling, MC and George Thorne, MD.

A 29-year-old male with epidermodysplasia verruciformis (EDV) was found to have normal cell mediated immunity. This patient is unique in that his initial lesions appeared at the site of the trauma, six months following a minor burn. Light and electron microscopic studies suggest a degenerative epidermal process. The lack of tonofilaments and cytoplasmic organelles on electron microscopic study may account for the abnormal clear cells seen with light microscopy. Attempts to culture the virus were unsuccessful. Both Vitamin-A acid and 5-fluorouracil were of no therapeutic value in paired comparison studies. Temporary clearing of his lesions in a localized area treated with 800r, single dose, Grenz-ray, was noted.

Localized Mycosis Fungoides

LTC John L. Aeling, MC and COL Donald D. Nuss, MC

Two patients with localized mycosis fungoides (MF) are reported. Both were treated with tumoricidal localized x-ray therapy and have remained free of both cutaneous and systemic disease for eight years, six months and one year, three months respectively. MF, histopathologically, is a polymorphus lymphoma and in this regard is similar to Hodgkin's disease. It is generally thought that MF begins in the skin with disseminated cutaneous lesions. These two cases demonstrate that the disease may be initially localized for a considerable period of time, and when the disease is treated at this stage with aggressive x-ray therapy, long term remissions can be achieved.

Multiple Hamartoma Syndrome

MAJ Wallace N. Weber, MC, MAJ Donald E. Clemons, MC, LTC John L. Aeling, MC and COL Donald D. Nuss, MC

Multiple hamartoma syndrome is a rare or rarely recognized autosomal dominant inherited disease manifesting benign and/or potentially malignant hamartomas in many organ systems. Four new cases from two families having multiple hamartoma syndrome (Cowden's disease) are presented. Their findings are discussed in light of previously described cases. Skeletal, pulmonary, and epidermal adnexal system involvements that have not been previously reported in this syndrome are presented.

Clinical Competence and Ward Attending Rounds

Frederic W. Platt, MD

When the American Board of Internal Medicine discontinued its oral examinations, the job of evaluating clinical competence was given to the individual residency programs. At Presbyterian Medical Center use is made of ward-attending rounds to teach and evaluate the clinical skills of interns and residents. During rounds, attending physicians observe 45-minute history and physical examinations, lead peer review of chart work, and share responsibility for 10-minute patient interviews. In the short interviews, attending physician and house staff physician alternate the roles of interviewer and observer. Clinical skills of many members of our house staff have been observed over several years. Data on the same physicians have been obtained by repeated observations and have been helpful to those individuals and to teaching program. These data have been accepted for clinical competence evaluation and seem to satisfy some of the ABIM requirements.

Liver Scan Defects in Lymphoma—The Effects of Irradiation

MAJ Kenneth D. Herbst, MC, Michael P. Corder, MD and Eugene T. Morita, MD

Twenty-one patients with lymphoma received radiotherapy to fields which included the left lobe of the liver. Liver scans using Technetium ^{99m} sulfa colloid were performed before and after radiotherapy. Two distinct irradiation-induced liver scan defects were noted: (1) an early, clearly delineated defect comparable to the radiation port and, (2) a generalized thinning of the left lobe of the liver. Seven of the patients were evaluated within six weeks after radiotherapy and five of these demonstrated the early radiation port defect. Seventeen of the twenty-one patients developed attenuation of the left lobe and this defect has persisted in all patients with followup of up to fifty-nine months. Since periodic liver scans are frequently performed in patients with lymphoma to evaluate for recurrent disease, these characteristic irradiation-induced liver scan defects must be recognized to avoid confusion with recurrent lymphoma and other causes of liver scan defects.

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Mount Airy Center Functioning

The $1.8 million East wing facility at the Mount Airy Psychiatric Center, 4455 East 12th Avenue, Denver was opened in mid-September, providing 50 beds in a new development as well as improved areas for new and expanded therapy programs for in-patients and out-patients. The bed count at Mount Airy remains 100. A 200 seat community room and an interdenominational chapel are included.

The chapel is furnished with sculpture, stained glass, and other art objects designed by Colorado artist Edgar Britton, and was dedicated to the memory of the late Murrell O. Matthews, past president and founding member of the Board of Trustees of the Mount Airy Foundation. It was given by his widow in his memory.

Spalding Director Appointed

Joon-Whee Kim, MD, former Assistant Chief of Rehabilitation Medicine at the Boston Veterans Administration Hospital, has been named Medical Director of Rehabilitation at the Spalding Rehabilitation Center, Denver.

Dr. Kim received his MD in Seoul, Korea, completed his internship at Ellis Hospital, Schenectady, New York, and fulfilled his Physical Medicine and Rehabilitation residency at the VA hospital in Boston. Dr. Kim is a member of the American Congress of Rehabilitation Medicine and the New England Society of Physical Medicine.

Boswick Takes Office

John A. Boswick, Jr., MD, Professor and Chairman, Hand Surgical Service at the University of Colorado Medical Center, has been elected to the office of Secretary for the American Association for the Surgery of Trauma for the term 1975-76.

Maybe the patient's self-diagnosis is right. He could have hay fever. But that bright red nasal mucosa, along with the thick discharge and excoriation around the nares, strongly suggests that the main problem is a cold. Hay fever or another form of allergic rhinitis may or may not be an underlying factor.

If a complete history and examination rule out allergic rhinitis, the long-term outlook will be a lot more favorable than his own "diagnosis" would have indicated.

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Whether it's a cold or an allergy, Dimetapp Extentabs® relieve stuffiness, drip and congestion.*

* INDICATIONS

Based on a review of this drug by the National Academy of Sciences — National Research Council and/or other information, FDA has classified the following indications as lacking substantial evidence of effectiveness as a fixed combination Dimetapp Extentabs are indicated for symptomatic relief of allergic manifestations of upper respiratory illnesses such as the common cold, seasonal allergies, sinusitis rhinitis, conjunctivitis and otitis In these cases it quickly reduces inflammatory edema, nasal congestion and excessive upper respiratory secretions thereby affording relief from nasal stuffiness and postnasal drip

CONTRAINDICATIONS: Hypersensitivity to antihistamines of the same chemical class Dimetapp Extentabs are contraindicated during pregnancy and in children under 12 years of age Because of its drying and thickening effect on the lower respiratory secretions Dimetapp is not recommended in the treatment of bronchial asthma Also Dimetapp Extentabs are contraindicated in concurrent MAO inhibitor therapy

WARNINGS: *Use in children:* In infants and children particularly, antihistamines in overdosage may produce convulsions and death

PRECAUTIONS Administer with care to patients with cardiac or peripheral vascular diseases or hypertension. Until the patient's response has been determined, he should be cautioned against engaging in operations requiring alertness such as driving an automobile, operating machinery etc Patients receiving antihistamines should be warned against possible additive effects with CNS depressants such as alcohol, hypnotics sedatives, tranquilizers, etc.

ADVERSE REACTIONS: Adverse reactions to Dimetapp Extentabs may include hypersensitivity reactions such as rash, urticaria leukopenia, agranulocytosis, and thrombocytopenia; drowsiness, lassitude giddiness, dryness of the mucous membranes tightness of the chest, thickening of bronchial secretions urinary frequency and dysuria palpitation, hypotension/hypertension, headache, faintness dizziness tinnitus incoordination visual disturbances, mydriasis, CNS-depressant and (less often) stimulant effect anorexia, nausea, vomiting, diarrhea constipation and epigastric distress

HOW SUPPLIED: Light blue Extentabs in bottles of 100 and 500.

Dimetapp Extentabs®

Dimetane® (brompheniramine maleate), 12 mg.; phenylephrine HCl, 15 mg.; phenylpropanolamine HCl, 15 mg.

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For the patient with a terminal illness, PAIN past, present, and future can dominate his thoughts until it becomes almost an obsession. The more he is aware of the pain he is now experiencing, the more difficult it is to erase his memory of yesterday's pain, and to allay his fearful anticipation of tomorrow's pain.

Surely the last thing this patient needs is an analgesic containing caffeine to stimulate the senses and heighten pain awareness. A far more logical choice is Phenaphen with Codeine. The sensible formula provides ¼ grain of phenobarbital to take the nervous "edge" off, so the rest of the formula can help control the pain more effectively. Don't you agree, Doctor, that psychic distress is an important factor in most of your terminal and long-term convalescent patients?

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Phenaphen with Codeine No. 2, 3, or 4 contains: Phenobarbital (¼ gr.), 16.2 mg. (warning: may be habit forming); Aspirin (2½ gr.), 162.0 mg.; Phenacetin (3 gr.), 194.0 mg.; Codeine phosphate, ¼ gr. (No. 2), ½ gr. (No. 3) or 1 gr. (No. 4) (warning: may be habit forming).

Indications: Provides relief in severer grades of pain, on low codeine dosage, with minimal possibility of side effects. Its use frequently makes unnecessary the use of addicting narcotics. **Contraindications:** Hypersensitivity to any of the components. **Precautions:** As with all phenacetin-containing products, excessive or prolonged use should be avoided. **Side effects:** Side effects are uncommon, although nausea, constipation and drowsiness may occur. **Dosage:** Phenaphen No. 2 and No. 3—1 or 2 capsules every 3 to 4 hours as needed; Phenaphen No. 4—1 capsule every 3 to 4 hours as needed. For further details see product literature.

ⒸIII Phenaphen with Codeine is now classified in Schedule III, Controlled Substances Act of 1970. Available on written or oral prescription and may be refilled 5 times within 6 months, unless restricted by state law.

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in Brief

A summary of AMA, medical & health news

American Medical Association / 535 North Dearborn Street / Chicago, Illinois 60610 / Phone (312) 751-6000 / TWX 910-221-0300

Two resolutions declaring the week of April 4, 1976, as National Rural Health Week have been introduced in the House and in the Senate. Rep. Ed Jones (D-Tenn.) and eight cosponsors introduced the House resolution, and Sens. Herman E. Talmadge (D-Ga.) and Robert J. Dole (R-Kan.) introduced the Senate version. Both resolutions were supported by the AMA.

Accreditation reports of the Joint Commission on Accreditation of Hospitals will remain confidential as a result of a consent decree filed in U.S. District Court in Chicago in which HEW agreed to stop making public the documents supplied to it by the JCAH for use in validation studies. The JCAH filed suit against HEW May 20, contending that the reports were protected by the 1972 Medicare amendments. HEW attorneys ruled that the reports were not protected and must be made public under the federal Freedom of Information Act. In the settlement, HEW agreed that, by law, accreditation letters and accompanying recommendations and comments are confidential and the JCAH agreed to continue supplying HEW with the reports as long as they are kept confidential.

An extension from Dec. 31, 1975, to June 30, 1976, has been granted in the AMA's PSRO Criteria Development Project, to allow sufficient time to conduct an evaluation study of the initial criteria document. The revised document is scheduled for publication in June, 1976. The original document, published last June, was developed by the AMA in cooperation with more than 30 medical specialty societies, under a grant from HEW, to serve as a reference for physicians in developing criteria for local PSROs and to assist in review processes of hospital admission certification, continued stay review, and health care evaluation studies.

The Robert Wood Johnson Foundation recently announced plans to finance a $14 million Rural Practice Project, which will assist teams of selected physicians and administrators set up approximately 25 community-based medical practices in rural areas throughout the U.S. The School of Medicine of the U. of North Carolina at Chapel Hill will administer the project for the foundation under the terms of a five-year grant of $2 million. The purpose of the project is to discover new approaches to the problem of health care access in rural America.

Nine AMA regional continuing medical education meetings are scheduled for 1976. They are designed to make AMA-sponsored Category 1 programs available to practicing physicians at times and places of convenience. The 1976 meetings are in Tulsa, Okla., Jan. 17-18; Denver, Colo., Feb. 27-28; Lexington, Ky., Mar. 17-20; Indianapolis, Ind., April 3-4; Detroit, Mich., April 3-4; Dallas, Tex., May 6-9; Jackson Hole, Wy., Sept. 3-5; Milwaukee, Wis., Sept. 11-12; and Portsmouth, N.H., Sept. 10-12.

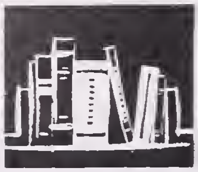
The Pharmaceutical Manufacturers Assn. filed suit Oct. 20 against HEW's implementation of the maximum allowable cost drug reimbursement program. The AMA had filed suit to block implementation of the MAC regulations on July 29.

"Medical Malpractice Law" is a new book for physicians, medical students, and attorneys, written by Angela Roddey Holder, JD. The 500-page book explains the principles of the physician's obligation to his patient throughout the course of the doctor-patient relationship and suggests ways in which physicians can avoid situations leading to lawsuits. It is available for $22.50 from John Wiley & Sons, Inc., 605 3rd Ave., New York, N.Y. 10016.

The AMA will present 20 two-day workshops entitled "Establishing Yourself in Medical Practice" during the 1975-76 term. The workshops are designed for young doctors planning to go into private practice and are sponsored by the AMA in cooperation with state medical societies. During 1975-76 workshops will be held in Tennessee, Pennsylvania, California, Illinois, Arizona, Louisiana, Texas, Washington, Kentucky, North Carolina, Georgia, Maryland, Washington, D.C., New Jersey, Ohio, South Carolina, Indiana, Michigan, Massachusetts, and Florida.

Available from AMA: "Physician-Hospital Relations, 1974," OP-425, is available for $4 each for 1-10 copies; $3.60 each for 11-49; and $3.20 for 50 or more from Order Dept., AMA Headquarters... "The Impaired Physician," a report highlighting a conference held last April on "The Disabled Doctor--Challenge to the Profession." Single copies are available from Dept. of Mental Health, AMA Headquarters.

11/75



THE BOOK CORNER

New books received are acknowledged in this section and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selection will be made for review in the interests of our readers and as space permits. Books are listed with advance data supplied by publishers. Prices quoted are not guaranteed. For further information, address queries to the publishers. Books here listed are available for lending from the Denver Medical Society Library.

Recent Acquisitions

Behavioral Pharmacology: Susan D. Iversen. New York, Oxford University Press, 1975. 310 p.

Bulfinch's Mythology; The Age of Fable, Chivalry and Legends of Charlemagne. New York, Crowell, 1970. 980 p. $5.30.

Classics of American Psychiatry: John P. Brady, ed. St. Louis, Mo., Warren H. Green, 1975. 281 p. $15.00.

Clinical Rheumatology; A Problem-Oriented Approach to Diagnosis and Management. Philadelphia, Lea & Febiger, 1975. 331 p. $14.00.

Cryosurgery in Ophthalmology: S. Percy Amolis, Chicago, Year Book, 1975. 181 p. $16.16.

Denver's Golden Days and Apothecary Palaces: Antique Bottle Collectors of Colorado, Inc. Denver, ABCC, Inc., 1971. 226 p. Gift.

Food, Nutrition and Diet Therapy: Marie V. Krause and Martha A. Hunscher. Philadelphia, Saunders, 1972. 718 p. $9.75.

Gastrointestinal Problems in the Infant: Joyce Gryboski. Philadelphia, Saunders, 1975. 811 p. (Major problems in clinical pediatrics, v. 13).

Hallucinations: Behavior, Experience, and Theory: R. K. Siegel and L. J. West. New York, Wiley, 1975. 322 p. $25.00.

Histopathologic Spectrum of Regional Enteritis and Ulcerative Colitis: Norman K. Mottet. Philadelphia, Saunders, 1971. 249 p. (Major problems in pathology, v. 2)

Leukemia: Frederick Gunz. 3rd ed. New York, Grune & Stratton, 1975. 841 p.

Lung Function: Assessment and Application: John E. Cotes. London, Blackwell, 1975. 619 p. $50.00.

Manual of Surgical Nutrition: American College of Surgeons. Committee on Pre and Postoperative Care. Philadelphia, Saunders, 1975. 527 p.

Medical Complications During Pregnancy: Gerard N. Burrow and Thomas F. Ferris. Philadelphia, Saunders, 1975. 962 p. $27.00.

Ocular Differential Diagnosis: Frederick H. Roy. 2nd ed. Philadelphia, Lea & Febiger, 1975. 612 p. $15.75.

Pathology of Muscle: John T. Hughes. Philadelphia, Saunders, 1974. 218 p. (Major problems in pathology, v. 4)

Peripheral Neuropathy: Peter J. Dyck, ed. Philadelphia, Saunders, 1975. 2 v. $108.00.

The Pharmacological Basis of Therapeutics: Louis S. Goodman and Alfred Gilman, eds. 5th ed. New York, Macmillan, 1975. 1704 p. $30.00.

Physician's Handbook of Nutritional Science: Roger J. Williams. Springfield, Ill., Thomas, 1975. 114 p. $9.75.

Polypoid Lesions of the Gastrointestinal Tract: Claude E. Welch. 2nd ed. Philadelphia, Saunders, 1975. 220 p. (Major problems in clinical surgery, v. 2, 2nd ed.)

Surgery in the Aged: Lazar J. Greenfield. Philadelphia, Saunders, 1975. 151 p. (Major problems in clinical surgery, v. 17) $11.25.

Surgery of the Billiary Tract: Bjorn Thorbjarnarson. Philadelphia, Saunders, 1975. 166 p. (Major problems in clinical surgery, v. 16)

MEDICAL SCHOOL NOTES

Waddell Honored at CU

William Rhoads Waddell, MD, professor of surgery and former chairman of the Department of Surgery, was honored October 10 with an all-day program during which a portrait of him was hung in the Department of Surgery Library, and such associates as Harry P. Ward, MD, acting vice president for health affairs and dean of the School of Medicine; Charles Halgrimson, MD, Claude Welch, MD; John Conger, MD, J. Cuthbert Owens, MD, and Thomas E. Starzl, MD, paid tribute to Doctor Waddell.

Doctor Waddell was graduated from Harvard Medical School in 1943, interned at Massachusetts General Hospital, and served there as a surgical resident. He served in the Navy, and was a research fellow in legal medicine. He came to the Medical Center in 1961 as professor and chairman in the Department of Surgery.

Family Medicine Center to Rise

A $559,700 family medicine center will be constructed near the School of Dentistry building to accommodate the resident training program of the Department of Family Medicine. A bid date of December 1976 with occupancy by January 1978 has been established.

The center will cover 7,600 square feet and will have 14 general and two pediatric examination rooms. Also to be included are x ray and laboratory facilities, reception and waiting areas, library, and consultation and staff offices. The center will have the capacity of handling 5,000 patients as compared with the 1,500 now seen.

McIntosh Receives Pediatric Award

Rawle McIntosh, head of pediatric nephrology at the Medical Center, has been selected by the American Academy of Pediatrics to receive the $3,000 E. Mead Johnson Award. The award is given for outstanding pediatric research, to any physician who has been out of medical school not more than 18 years, and has dominated the field of research.

Doctor McIntosh received his MD in 1963 from New York Medical College, and took his pediatric residency at the University of California, San Francisco, and at Stanford University. He was a postdoctoral fellow at the University of California, Los Angeles, and a research associate at La Rabida-University of Chicago Institute. He joined the University of Colorado Medical Center in 1973.

UCMC Construction Plans Approved by CU Regents

Program plans for an addition to the University of Colorado School of Nursing building and for remodeling and renovating two floors of the Colorado Psychiatric Hospital have been approved by the CU Board of Regents. The $1,759,609 nursing school addition will be a three-story building plus basement which will be constructed between the current structure and the Denison Memorial Library. The new building is necessary to accommodate the increased number of continuing and general education courses, students, and research programs which have occurred during the past five years. The building, tentatively slated to be completed in November, 1977, will provide space for teaching, administration, faculty and support services. The project has been included in the 1976-77 UCMC capital budget request, with $616,158 allocated to the state and $1,143,451 to the federal government.

Also included in the 1976-77 UCMC capital budget request is the $438,000 remodeling and renovation of the second and third floors of CPH. The former inpatient wards will be converted to laboratory, treatment, office and supporting service areas.

Brettell Named to Head Family Medicine

Herbert Brettell, MD, professor of family medicine, medicine and preventive medicine at the University of Colorado School of Medicine, has been named chairman of the CU Department of Family Medicine. The CU Board of Regents approved the appointment, retroactive to Sept. 1, 1975, on Oct. 16. Doctor Brettell, the former head of the CU Division of Family Practice, was named acting chairman when the division was given departmental status in April, 1975.

A 1950 graduate of the University of Rochester School of Medicine, Minnesota, Doctor Brettell did his internship at the Vanderbilt University Hospital, Nashville, Tenn., and his residencies at the CU Medical Center. After spending 16 months in private practice in Logan, Utah, he returned to UCMC in 1956 as an instructor in medicine.

The new department chairman is a fellow of the American College of Physicians and the American College of Clinical Pharmacology and Chemotherapy.

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And as you well know, no one can guarantee your physical well-being. Should a disability keep you from your practice, the Colorado Medical Society's Disability Income Protection Plan will provide regular monthly benefits. They are paid directly to you to use as you see fit. What's more, these benefits are *tax-free* under current federal income tax laws. And you can count on Mutual of Omaha to provide personal service to help you select the right plan.

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IMPORTANT INFORMATION: *This is a Schedule V substance by Federal law; diphenoxylate HCl is chemically related to meperidine. In case of overdosage or individual hypersensitivity, reactions similar to those after meperidine or morphine overdosage may occur; treatment is similar to that for meperidine or morphine intoxication (prolonged and careful monitoring). Respiratory depression may recur in spite of an initial response to Nalline® (nalorphine HCl) or Narcan® (naloxone HCl) or may be evidenced as late as 30 hours after ingestion. LOMOTIL IS NOT AN INNOCUOUS DRUG AND DOSAGE RECOMMENDATIONS SHOULD BE STRICTLY ADHERED TO, ESPECIALLY IN CHILDREN. THIS MEDICATION SHOULD BE KEPT OUT OF REACH OF CHILDREN.*

Indications: Lomotil is effective as adjunctive therapy in the management of diarrhea.

Contraindications: In children less than 2 years, due to the decreased safety margin in younger age groups, and in patients who are jaundiced or hypersensitive to diphenoxylate HCl or atropine.

Warnings: Use with special caution in young children, because of variable response, and with extreme caution in patients with cirrhosis and other advanced hepatic disease or abnormal liver function tests, because of possible hepatic coma. Diphenoxylate HCl may potentiate the action of barbiturates, tranquilizers and alcohol. In theory, the concurrent use with monoamine oxidase inhibitors could precipitate hypertensive crisis. In severe dehydration or electrolyte imbalance, withhold Lomotil until corrective therapy has been initiated.

Usage in pregnancy: Weigh the potential benefits against possible risks before using during pregnancy, lactation or in women of childbearing age. Diphenoxylate HCl and atropine are secreted in the breast milk of nursing mothers.

Precautions: Addiction (dependency) to diphenoxylate HCl is theoretically possible at high dosage. Do not exceed recommended dosages. Administer with caution to patients receiving addicting drugs or known to be addiction prone or having a history of drug abuse. The subtherapeutic amount of atropine is added to discourage deliberate overdosage; strictly observe contraindications, warnings and precautions for atropine; use with caution in children since signs of atropinism may occur even with the recommended dosage. Use with care in patients with acute ulcerative colitis and discontinue use if abdominal distention or other symptoms develop.

Adverse reactions: Atropine effects include dryness of skin and mucous membranes, flushing, hyperthermia, tachycardia and urinary retention. Other side effects with Lomotil include nausea, sedation, vomiting, swelling of the gums, abdominal discomfort, respiratory depression, numbness of the extremities, headache, dizziness, depression, malaise, drowsiness, coma, lethargy, anorexia, restlessness, euphoria, pruritus, angioneurotic edema, giant urticaria, paralytic ileus, and toxic megacolon.

Dosage and administration: ***Lomotil is contraindicated in children less than 2 years old.*** Use only Lomotil liquid for children 2 to 12 years old. For ages 2 to 5 years, 4 ml. (2 mg.) t.i.d.; 5 to 8 years, 4 ml. (2 mg.) q.i.d.; 8 to 12 years, 4 ml. (2 mg.) 5 times daily; adults, two tablets (5 mg.) t.i.d. to two tablets (5 mg.) q.i.d. or two regular teaspoonfuls (10 ml., 5 mg.) q.i.d. Maintenance dosage may be as low as one fourth of the initial dosage. Make downward dosage adjustment as soon as initial symptoms are controlled.

Overdosage: Keep the medication out of the reach of children since accidental overdosage may cause severe, even fatal, respiratory depression. Signs of overdosage include flushing, hyperthermia, tachycardia, lethargy or coma, hypotonic reflexes, nystagmus, pinpoint pupils and respiratory depression which may occur 12 to 30 hours after overdose. Evacuate stomach by lavage, establish a patent airway and, when necessary, assist respiration mechanically. A narcotic antagonist may be used in severe respiratory depression. Observation should extend over at least 48 hours.

Dosage forms: Tablets, 2.5 mg. of diphenoxylate HCl with 0.025 mg. of atropine sulfate. Liquid, 2.5 mg. of diphenoxylate HCl and 0.025 mg. of atropine sulfate per 5 ml. A plastic dropper calibrated in increments of ½ ml. (total capacity, 2 ml.) accompanies each 2-oz. bottle of Lomotil liquid.

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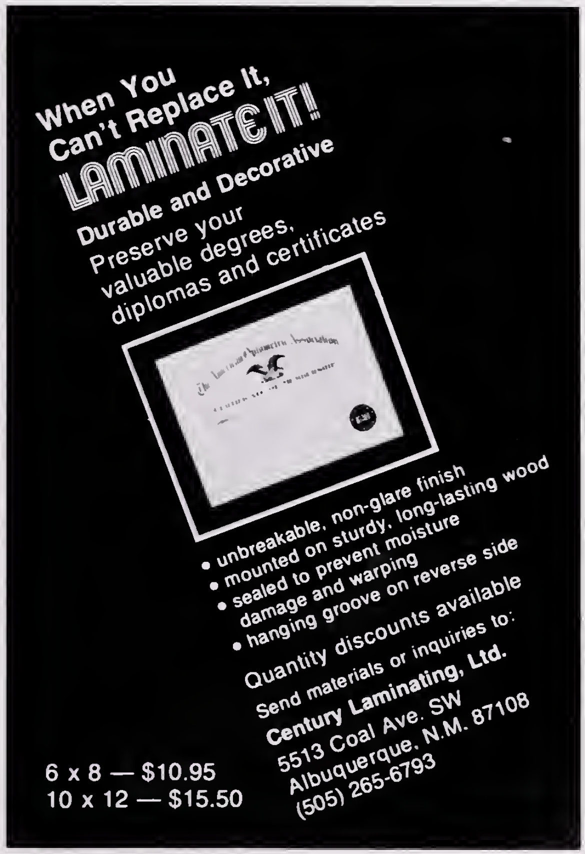

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OBITUARIES

Colorado

Vern G. LaTourette, MD, died Friday, October 31 at the University of Maryland Hospital, Baltimore. He had gone to that institution for treatment of leukemia from which he had been suffering for the past ten months.

Born in Buckeye, Arizona, April 10, 1922, he attended Arizona State University and the University of Notre Dame, then received his MD from New York Medical College in 1950. He interned at Fitzsimons Army General Hospital from 1950 to 1951, then entered the Radiological Training Program of the University of Colorado Medical Center in 1951. After completing his training in 1955 he became radiologist at Mercy Hospital, Denver.

He was a Diplomate of the American Board of Radiology and was a fellow of the American College of Radiology. He was a member of the Radiological Society of North America; the Society of Nuclear Medicine, and the Rocky Mountain Radiological Society. He served as president of the Rocky Mountain Chapter of the Society of Nuclear Medicine in 1967, president of the Rocky Mountain Radiological Society in 1972-73, and president of the Colorado Chapter of the American College of Nuclear Medicine in 1974-75. He was a member of the Denver and Colorado Medical societies and of the American Medical Association.

He was lieutenant (j.g.) in the U.S. Naval Reserve from 1943-46, and was a first lieutenant in the Army in 1951.

Doctor LaTourette was married to Margaret B. Woolfolk, May 27, 1945 in Yonkers, New York. She later became a physician and practiced Pediatrics in the Denver area.

Doctor LaTourette was somewhat of a pioneer in the use of ultrasound in medical diagnosis. Mercy Hospital was the first private hospital in the Denver area to install the required equipment, under his direction.

He is survived by his widow Margaret LaTourette, MD, four sons, Steven P., James R., John R., and Thomas E. of Denver; two sisters, Mrs. Frances Nichols, Mesa, Arizona, and Mrs. Elizabeth Brannan, Tempe, Arizona, and a granddaughter.

Montana

Donald J. MacDonald, MD, general surgeon and internist of Billings, died April 1, 1975 at the age of 66. Doctor MacDonald began his practice in Billings in 1940, and retired in 1974. He had been a member of the Montana Medical Association since 1940, and a member of the American Medical Association. He is survived by his widow, two sons, two daughters, and four sisters.

John W. Schubert, MD, of Lewistown, died September 18 in Great Falls at the age of 69, following a lengthy illness. Doctor Schubert had been Fergus County health officer since 1945, and practiced in Lewistown.

Doctor Schubert was born in Great Falls, was graduated from Great Falls High School and the University of Montana where he received a degree in pharmacy. His medical degree was awarded by the University of Minnesota in 1937.

At this time he established a practice in Hardin where he served until 1945 when he moved to Lewistown. Doctor Schubert was a member of the Montana and American Medical associations, and the Academy of General Practice.

He is survived by his widow, La Verne, and sons John, Buena Ventura, Colombia; Dr. Timothy, Yonkers, NY, and William, Missoula, and daughters Mary Galusha, Escondido, California, and Madelle Atkinson, Maseru Lesotho, South Africa.

Dewitt Edward Harrison, 58, of Polson, Montana, died September 28, 1975 when a small farm tractor capsized on him. Doctor Harrison had moved to Montana from Elyria, Ohio in 1973, and had been a member of the Montana Medical Association and Flathead Medical Society. He is survived by his widow and two sons.

Clayton F. Hogeboom, MD, of Baker, Montana, died August 25, 1975 at the age of 73. He had been a member of the Montana Medical and the American Medical associations.

Arthur J. Movius, Jr., MD, Billings surgeon, whose father founded the Billings Clinic, died April 8, 1975 at the age of 64. A fellow of the American College of Surgeons and the American Society of Abdominal Surgeons, he had been a member of the Montana Medical and American Medical Associations since 1942. He is survived by his widow, two sons, two brothers, two sisters, two step-sons, two step-daughters, and five grandchildren.

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WANT ADS

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PHYSICIAN WANTED. Man or woman. If you are looking for a change in your life style, then collaborate with a Ph.D. Molecular Biologist in research or Medical Services. Long-term association contemplated. Phone evenings and weekends collect, between 8 p.m. and 11 p.m.: (212) 675-7398 or Write: Ronald Friedman, Ph.D., P.O. Box 261, Bronx, New York 10463. 775-5-6B

INTERNIST NEEDED for active 96-bed GM&S Veterans Administration Hospital, well-equipped and staffed, with excellent library and consultants. Must be Board-qualified with solid medical background. Salary: $30-36,000; excellent fringe benefits; will pay travel and moving expenses; housing on hospital grounds. Equal opportunity employer; licensure required in one of the fifty states or District of Columbia. Abundant outdoor recreation; pleasant climate with clean air in attractive peaceful western city of 10,000. Inquire: Norman C. Jorgenson, MD, Chief of Staff, or T. L. Massey, Hospital Director, VA Hospital, Miles City, Montana 59301, or call collect: (406) 232-3060. 975-6-4B

FAMILY PRACTITIONER—BRAND NEW FACILITY located 20 minutes from ski area, and 25 minutes from Denver. Salary negotiable. Contact: G. E. Cimochowski, MD, P.O. Box 1856, Evergreen, Colorado 80439 or call: (303) 674-7694. 1175-5-2

WANTED: OB-GYN and General Surgeon, Board certified or eligible, for university town in Southwestern New Mexico mining community, in seven man multispecialty group. Prefer American graduate. Write: Raymond T. Smith, Clinic Manager, Med Square Clinic, 114 West 11th Street, Silver City, New Mexico 88061. 1075-4-3B

PHYSICIANS ASSOCIATE—Family Practice. Duke University graduate 1973 wants to relocate in Denver area. For further information write: Mr. James Ellis, 1401 Golf Road, Waukegan, Illinois 60085. 1175-2-3B

NEEDED: GENERAL AND THORACIC SURGEON to join Surgical Department of Great Falls Clinic, a 28-doctor multispecialty group. Contact: Administrator, Great Falls, Clinic, 1220 Central Avenue, Great Falls, Montana 59403. 1175-10-2B

GRAND JUNCTION—FOR RENT or LEASE: Offices in high-ranking location near St. Mary's Hospital, X-ray and laboratory adjacent. Call: (303) 243-0726 or write: H. R. Bull, MD, Suite 10, 2232 North 7th, Grand Junction, Colorado 81501. 1175-1-3B

CERTIFIED PHYSICIAN'S ASSISTANT desires employment with physician (Family Practice preferred) Colorado area of choice—other states considered. References and resume upon request. Write: Lance Lewandowski, 1724 Ashley Hall Road, Apt. M, Charleston, South Carolina 29407. 1175-3-3B

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POSITIONS AVAILABLE for Board Certified/Eligible General Internists for addition to multi-specialty group beginning November 1975. Additional position open for Internist/Gastroenterologist in January 1976. Contact: Colorado Permanente Medical Group, Suite 706, 2045 Franklin Street, Denver, Colorado 80205. 975-10-3

WANTED: Used equipment for family practice, including examining table. Call: Peter Monheit, MD. (303) 771-1647. 975-11-3

POSITIONS AVAILABLE FOR PSYCHIATRISTS, adult and child, full time, for growing Colorado HMO beginning 1976. Emphasis on eclectic, brief, and group therapy. Salary negotiable. No private practice allowed. Good fringe benefits. Contact: W. L. Reimers, MD, 2045 Franklin Street, Denver, Colorado 80205. 975-12-4

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VAIL, COLORADO OPENING for General Practitioner or Family Practitioner with an interest in Trauma and Orthopedics. Join a Family Practitioner for the 1975-76 ski season, with an opportunity for a permanent position. For details write G. R. Dooher, MD, Box 2086, Vail, Colorado 81657, or call: (303) 476-2129 after 7 p.m. 975-13-3

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ME 35, currently established in Denver, some training in Internal Medicine, but Family Practice oriented, seeks to relocate in rural Colorado community; has had several years rural health care experience. Some financial backing required. Please give maximum details first letter. Write: Box 1275-5-1B, c/o Rocky Mountain Medical Journal, 1601 E. 19th Avenue, Denver, Colorado 80218. 1275-5-1B

WANTED: Old brass microscopes, microscope parts and accessories, books, and other literature about microscopes. Contact: Wendell P. Stampfli, MD, Salida Hospital, Salida, Colorado 81201, or Call evenings: (303) 395-2397. 1275-6-1B

HAWAII. Small hospital, rural Oahu, needs semi-retired radiologist, part-time. Good pay for hours worked. Beautiful beaches, climate, etc. Write for details to: Administrator, Kahuku Hospital, Kahuku, Hawaii 96731. 1275-7-3B

FOR LEASE: Established medical office location at 2929 South Broadway, Englewood, Colorado. Complete with current patient files, now available. Contact: Dr. or Mrs. Maercklein at: (303) 789-9571 for details. 1275-8-2B

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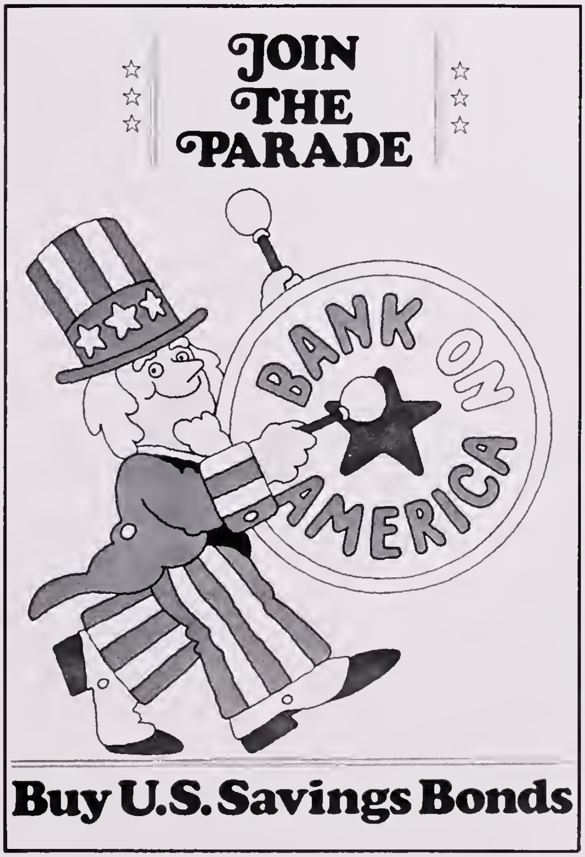

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Opinion & Dialogue

Should a specially prepared package insert be made available to patients?

Dr. Alexander M. Schmidt
Commissioner,
Food and Drug
Administration

The idea of a so-called patient package insert has been around for a long time. Many physicians already use written instruction sheets to provide patients with information about the drugs they are taking. And some physicians give verbal instructions; but in too many instances these are what I call eye-glazing exercises. I have seen patients sit with glazed eyes listening to a rapid-fire lecture by a hurried physician who has 20 people out in his waiting room. These patients aren't given sufficient understanding and therefore do not follow instructions. So I think the idea of an official package insert for patients is a good one. Perhaps we should really think of this kind of information simply as an extension of drug labeling.

The benefits of patient involvement

Many physicians may not realize how frequently a patient obtains his drug information from Aunt Tillie or the next door neighbor. And this information is almost always bad or irrelevant to the case at hand. Furthermore, the incentive to go along with a prescribed program is slim if the only reading matter the patient receives, along with his prescription, is a bill.

As an educator I am impressed by the principle that the best way to get someone to do something is to involve him in the process. So the

Dr. James H. Sammons
Executive Vice President
of the American
Medical Association

I think there are advantages as well as some real disadvantages in a patient package insert. When you begin to use semi-medical or medical terms to describe complications or possible sequelae of disease or treatment, you may frighten the patient—particularly since the more highly sophisticated patient is not the one who is going to read the insert. The patient who will read it is the one most susceptible to fright and confusion by the language.

On the positive side, a package insert will probably give the patient better insight into why he is being treated the way he is, and it may give the physician a little bit more time. But it does not remove from the physician the need or obligation to explain the insert.

Some pitfalls in the inclusion of side effects

Certainly a patient should be warned of the possibility of serious side reactions—to know what the real dangers are. But it doesn't do a bit of good to indicate that a patient on oral penicillin may develop a rash, itching, or a drop in blood pressure. Or that he may faint. I think the real danger is that fright engendered by the insert may possibly outweigh the potential good.

main purpose of drug information for the patient is to get his cooperation in following a drug regimen.

Preparation and distribution of patient drug information

We would hope to amass information from physicians, medical societies, the pharmaceutical industry and centers of medical learning. The ultimate responsibility for uniform labeling must, however, rest with the Food and Drug Administration. There is nothing wrong with this agency saying, "this information is generally agreed upon and therefore it should be used," as long as our process for getting the information is sound.

Distribution of the information is a problem. In great measure it would depend on the medication in question. For example, in the case of an injectable long-acting progesterone, we would think it mandatory to issue two separate leaflets—a short one for the patient to read before getting the first shot and a long one to take home in order to make a decision about continuing therapy. In this case, the information might be put directly on the package and not removable at all. But for a medication like an antihistamine this information might be issued separately, thus giving the physician the option of distribution. This could preserve the placebo use, etc.

It is in the distribution of patient information that the pharmacist may get involved. As professionals and members of the health-care team and as a most important source of drug information to patients, pharmacists should be responsible for keeping medical and drug records on patients. It is also logical that they should distribute drug information to them.

Realistic problems must be considered

We have to expect that the introduction of an information device will also create new problems. First, how can we communicate complex and sophisticated information to people of widely divergent socio-economic and ethnic groups? Second, what will we say? And third, how can we counteract the negative attitude of many physicians toward any outside influence or input? Hopefully the medical profession will respond by anticipating the problems and helping to solve them. Assuming we can also solve the difficulty of communicating information to diverse groups throughout the United States, our remaining task will be the inclusion of appropriate material.

What information is appropriate?

In my opinion, technical, chemical and such types of material should not be included. And there is no point in the routine listing of side effects like nausea and vomiting which seem to apply to practically all drugs, unless it is common with the drug. However, serious side effects should be listed, as should information about a medication that is potentially risky for other reasons.

Other pertinent information might consist of drug interactions, the need for laboratory follow-up, and special storage requirements. What we want to include is information that will help increase patient compliance with the therapy.

Positive aspects of patient drug information

Labeling medication for the patient would accomplish a number of good things: the patient could be on the lookout for possible serious side effects; his compliance would increase through greater understanding; the physician would be a better source of information since he would be freer to use his time more effectively; other members of the health-care team would benefit through patient understanding and cooperation; and, finally, the physician-patient relationship would probably be enhanced by the greater understanding on the part of the patient of what the physician is doing for him.

Only the doctor can remove that fear by 20 or 30 minutes of conversation.

I'm not suggesting that we withhold any information from the patient because, first of all, it would be totally dishonest and secondly, it would defeat the very purpose of the insert. I do think that a patient on the birth control pill should know about the incidence of phlebothrombosis.

If you're going to tell a patient the incidence of serious adverse reactions, then you have to tell him that a concerned medical decision was made to use a particular medication in his situation after careful consideration of the incidence of complications or side effects.

Emotionally unstable patients pose a special problem

There are patients who, because of severe emotional problems, could not handle the information contained in a patient package insert. Yet if we are going to have a package insert at all, we just can't have two inserts. I think we might simply have to tell the families of these patients to remove the insert from the package.

Legal implications of the patient package insert

Just what effect would a patient package insert have on malpractice? We could try to avoid any legal implications by pointing out that the physician has selected a particular medication because, in his professional judgment, it is the treatment of choice. For instance, you can't tell everyone taking antihistamines not to work just because a few patients develop extreme drowsiness which can lead to accidents. And what about the very small incidence of aplastic anemia rarely associated with chloramphenicol? If, based on sensitivity studies and other criteria, we decide to employ this particular antibiotic, we do so in full knowledge of this serious potential side effect. It's not a simple problem.

How do we handle an insert for medication used for a placebo effect?

With rare exceptions, physicians no longer use medications for a placebo effect. This question does raise the issue of how a patient may react to receiving a medication without a package insert.

Preparation of the package insert

The development of the insert ought to be a joint operation between physicians, the pharmaceutical industry, the A.M.A. and the F.D.A.

I view the A.M.A.'s role as a coordinator or catalyst. It is the only organization through which the profession as a whole, irrespective of specialty, can speak. It has relatively instant access to all the medical expertise in this country. And it can bring that professional expertise together to ensure a better package insert. The A.M.A. can work in conjunction with the industry that has produced the product and which is ultimately going to supply the insert.

I don't think we should rely, or expect to rely, on legislative committees and their nonprofessional staffs to make these decisions when it is perfectly within the power of the two groups to resolve the issues in the very best American tradition—without the government forcing us to do it. I think the F.D.A. has to be involved, but I'd like them to become involved because they were asked to become involved.

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